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A STUDY OF VACUUM  
EXTRACTOR DELIVERIES\*

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THE VACUUM extractor or "ventouse", as perfected by Tage Malmström<sup>1</sup> of Sweden in 1954 and modified by him in 1957, is already replacing the obstetric forceps in many European centres to a great extent, and is now being tested in certain clinics of North America. This instrument, with its new approach to the age-old problem of dystocia, is a valuable addition to the obstetrician's armamentarium. To justify this statement, it is emphasized that the greatest appeal of the vacuum extractor is in its absolute safety for mother and child, even in the hands of the tyro obstetrician.

HISTORY

For many centuries the physician has had to face the problem of effecting delivery in the presence of dystocia, especially when fetal distress threatens. There is a long history of operative intervention in these situations. Excluding Cesarean section, the following methods of aiding vaginal delivery have been advocated: pubiotomy or symphysiotomy as perfected by Zorato, which is popular mainly in South America; extraction using obstetrical forceps, developed by the Chamberlen family in the seventeenth century and which, with modifications, is still the most popular in the world today; scalp traction with Willett forceps, not in great use because of the frequency of scalp lacerations which result; and suction traction by the creation of a vacuum.

The first use of vacuum extraction was recorded in 1706 by Yonge, who used a cupping glass to create an artificial caput on the infant's head. This approach was revived by Simpson in 1849, when he devised a rubber suction cup attached to a long brass syringe to develop suction. In 1890 McCahey commented on the value of a rubber cup on a long solid handle (similar to the plumber's vacuum pump of today) to grasp the fetal head. Through the years the idea of scalp traction by means of

suction was kept alive by such men as Torpin, Couzigou and Koller, Finderle<sup>4</sup> in 1952, and Malmström<sup>1</sup> in 1954. Finderle's suction apparatus consisted of a horn rather than a cup, and seems to have been rather traumatic to the fetal scalp. Malmström's cup designed in 1954 was made of rubber and metal, but was modified in 1957 to the all-metal cup in current use.

DESCRIPTION

The vacuum extractor consists of a metal cup, available in three different sizes, attached by rubber tubing to a pump which creates suction. Evelbauer<sup>2</sup> replaced the hand pump with an electric motor, and claims that he can create maximum suction in one to two minutes, as opposed to the eight or ten minutes required with the hand pump. Figs. 1 and 2 describe the principle of operation and design of the vacuum extractor.

As will be demonstrated below, the suction cup creates an artificial caput succedaneum on the baby's scalp, which, because of its appearance, is called a "chignon". This chignon disappears rapidly, at times leaving a dusky ring corresponding to the edge of the suction cup; it is usually gone when the baby and its mother are discharged from hospital.

INDICATIONS

The indications for the application of the vacuum extractor are similar to those for the obstetrical forceps, the exceptions, as stated by Chalmers and Fothergill,<sup>5</sup> being: face presentation; the after-coming head in breech presentations; a transverse lie; and acute fetal distress. However, to compensate for these limitations, the vacuum extractor has the distinct and unique advantage that it can be applied before the cervix is fully dilated. This allows some of the following problems to be dealt with effectively:

1. Deep mid-pelvic arrest accompanied by posterior or transverse presentations.
2. Uterine inertia or atony.
3. Marginal placenta previa, where the descent of the head is required to control bleeding.
4. Abruptio placentae with a dead fetus, where the termination of labour is desirable for maternal safety.

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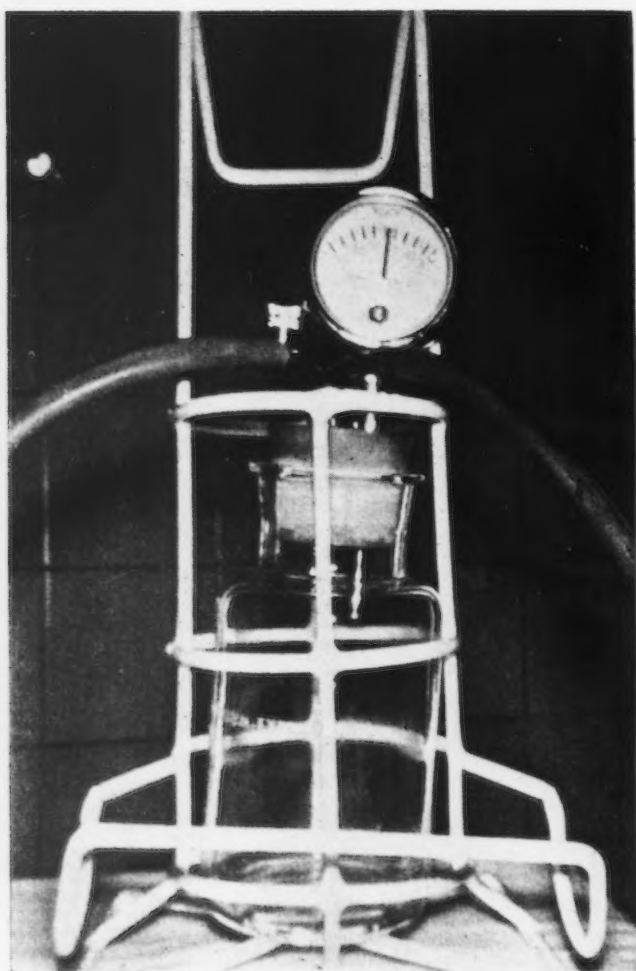


Fig. 1.—Vacuum extractor glass container with vacuum gauge and connections in metal case.

5. A delivery of the second child of a twin birth when his or her head remains high.

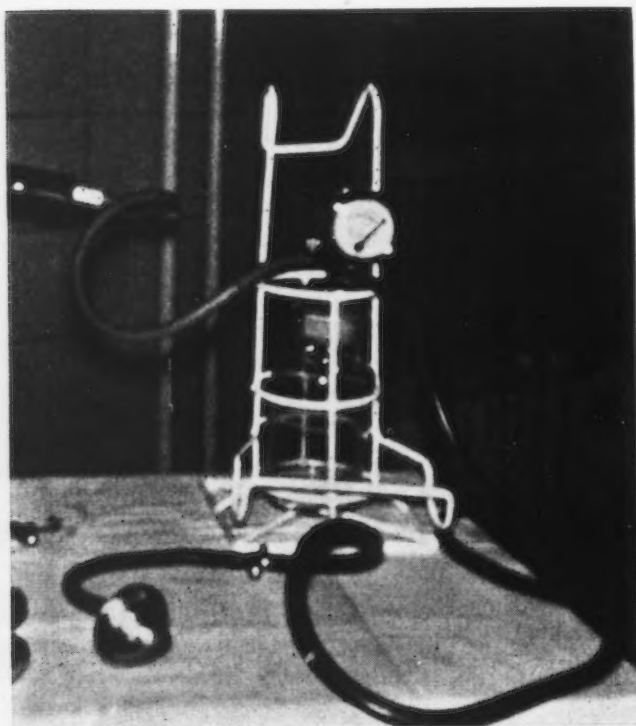


Fig. 2.—The long rubber tube is shown attached to the traction cup, and the short rubber tube to the suction pump.



Fig. 3.—The appearance of baby's head immediately after delivery. Note chignon.



Fig. 4.—The appearance of baby's head six days after delivery.

6. To overcome delay in a frank breech presentation, the extractor may be applied to the buttock.

There has been a reduction in the rate of Cesarean sections in some hospitals using the vacuum extractor; for example, in Berggren's<sup>3</sup> series the Cesarean rate dropped from 2.4% to 1.4%. However, the present author does not believe that the vacuum extractor should be used to hasten normal labour, as advocated by Pigeaud in 1957; or that it is necessary to wait for full dilatation of the cervix as reported in the recent series by Tricomi, Amorosi and Gottschalk;<sup>6</sup> or that the vacuum extractor is a complete substitute for forceps, as suggested by Finderle.<sup>4</sup> Our opinion, shared by Malmström<sup>1</sup> and Evelbauer,<sup>2</sup> is that the vacuum extractor may be used in preference to obstetrical forceps in most instances.

Many physicians may be reluctant to use the vacuum extractor because they fear that the suction exerted over the longitudinal sinus and the fon-

tanelles may result in possible hemorrhage or brain damage. However, in our experience this has not happened, and a review of the literature shows that Berggren<sup>3</sup> has a series of 100 cases with no neonatal mortality; Chalmers and Fothergill<sup>5</sup> have a series of 100 cases with one neonatal death in a premature twin; Tricomi, Amorosi and Gottschalk's series of 50 cases had no neonatal deaths; Evelbauer<sup>2</sup> has a series of 250 cases with no neonatal deaths, and in his follow-up survey of four years no evidence of cerebral damage was discovered. There is absolutely no danger for the mother in the use of the vacuum extractor, unless an area of cervix or vaginal wall is inadvertently caught in the cup during application. To date, the above-mentioned authors have not reported this occurrence, or any damage to the vaginal sulcus or uterus. It is not anticipated that the specialist who has become adept and highly competent in the use of forceps will accept this new trend easily. However, this method has many advantages because the vacuum extractor does not involve so many difficult maneuvers as the forceps, and there is not such a high incidence of fetal and maternal trauma.

#### APPLICATION

The vacuum extractor is applied after the patient has been prepared, draped and placed in the lithotomy position. Depending on cervical dilatation and station of the head, the largest cup possible, lubricated with green soap solution or Dettol cream, is gently introduced into the vagina and any pressure that may be necessary in introducing it is directed toward the perineum. The cup is then maneuvered against the fetal head where it is placed over the posterior fontanelle or any existing caput succedaneum. Now, an assistant operates the hand pump until a negative pressure of 0.2 kg./cm.<sup>2</sup> is indicated on the manometer. At this point it is exceedingly important to check the rim of the cup to be certain that no cervix or vaginal mucosa has been caught in the extractor. With the cup properly in position, negative pressure is built up in increments of 0.2 kg./cm.<sup>2</sup> every two minutes until a vacuum of 0.8-1.0 kg./cm.<sup>2</sup> is created. This usually takes eight to ten minutes; Evelbauer<sup>2</sup> states that the pressure can be attained in two to five minutes. In our experience the slower production of the vacuum produces a better chignon. If the patient is apprehensive, anesthesia in the form of trichlorethylene (Trilene), nitrous oxide or a pudendal nerve block may be used while the cup is being applied, after which the patient is allowed to awaken.

Certain important principles must be observed to obtain a successful extraction. As with forceps, the direction of pull must be in the axis of the birth canal (Figs. 5-7).

The operator must maintain flexion of the head with his free hand; this is especially important



Fig. 5.—The vacuum cup is applied and traction downwards commenced.

when one is unable to place the cup directly over the posterior fontanelle, because of incomplete dilatation or unfavourable presentation. Traction should always be in synchronization with uterine contractions. Fauvet and Finkbeiner have a large series of cases with continuous traction showing an increased incidence of scalp damage. If one of the prime indications for use of the vacuum extractor is uterine inertia, how does one avoid continuous traction? According to Caldeyro-Barcia and Alvarez, there is no evidence of reflex stimulation of the uterine pacemakers by increased cervical pressure. Clinically, however, rupture of membranes and use of the vacuum extractor definitely seem to increase uterine contractions. Huber be-



Fig. 6.—Traction continued upwards.



Fig. 7.—Traction completed.

lieves that a reflex response is produced by pressure on Frankenhauser's plexus. In any case, if traction is not successful in starting contractions, it is perfectly safe, according to Wolf, to use uterine stimulants such as Pitocin drip, after ensuring that there is no cephalo-pelvic disproportion. In marginal placenta previa limited continuous traction may be used until the head has descended sufficiently to act as a tamponade. Frequently, traction alone will overcome most rotation problems. When the descending head reaches the pelvic floor, it will physiologically rotate to an anterior or posterior position; should this fail to occur, there is an orientation knob on the cup which facilitates manual rotation to the desired direction. Pudendal block is an ideal anesthetic for use with the vacuum extractor. Deep general anesthesia will interfere with contractions, hence is not to be used for these deliveries. We occasionally use nitrous oxide to tide the patient over each contraction, and episiotomy is carried out whenever required.

#### PRESENT SERIES

In this series we used the vacuum extractor mainly in instances of fetal distress or failure of progress. During our period of "growing pains", the cup became detached during traction, but the following precautions have reduced the occasions for reapplication to a minimum: the use of the largest cup possible; taking time to create a good chignon; and keeping the head well flexed and properly rotated.

In this series 28 of the patients were primigravidae and 22 were multigravidae.

The distribution of neonates according to weight is shown in Table I. The smallest baby weighed 5 lb. 10 oz. and the largest baby weighed 10 lb. 3 oz.

TABLE I.—DISTRIBUTION OF NEONATES ACCORDING TO WEIGHT

5 to 6 lb.....	3
6 to 7 lb.....	9
7 to 8 lb.....	18
8 to 9 lb.....	10
9 to 10 lb.....	8
10 to 11 lb.....	2

Their distribution according to station in pelvis was: high, none; mid, 23 (13 fully dilated; 10 not fully dilated); low, 27.

The indications for use of the vacuum extractor are given in Table II.

TABLE II.—INDICATIONS FOR USE OF VACUUM EXTRACTOR

Mid-pelvic delay.....	23 cases
Outlet delay.....	16 "
Fetal distress.....	5 "
Uterine inertia.....	4 "
Placenta previa.....	1 "
Interventricular septal defect in mother.....	1 "

This classification is difficult because often two indications are present in the same case. The term "mid-pelvic delay" indicates that there was delay in the first stage, either with incomplete dilatation or with complete dilatation, and no progress because of abnormal position. The most common problem was deep transverse arrest or posterior position, but placenta previa and fetal distress each appears once in this group.

"Outlet delay" refers primarily to those cases in which the cervix was fully dilated but spontaneous delivery did not occur within one hour after the patient had been on the delivery table. Most of these women had borderline pelvic measurements or rigidity of the soft parts. Uterine atony and fetal distress have been kept separate where these were the principal reasons for using the vacuum extractor.

*Anesthesia.*—The anesthesia used was caudal in one case, pudendal block in 10 cases and nitrous oxide in 39 cases. We prefer pudendal block, perhaps combined with nitrous oxide in the very apprehensive patient, but an epidural block may be used.

*Vacuum and cup size.*—Slow build-up of vacuum to 0.8 kg./cm.<sup>2</sup> or 1.0 kg. over approximately ten minutes gave the best chignon, and hence better traction, when the largest size cup possible was used.

*Complications.*—There were no maternal complications. There was scalp excoriation in one infant and respiratory depression in two infants, both of whom showed signs of fetal distress.

#### COMMENT

In six patients, delivered early in this experience, the vacuum extractor was used for mid-pelvic rotation and delivery, but the cup became detached when the head was on the perineum, and delivery was completed with low forceps. This was not termed a failure, because the primary difficulty had been overcome, and the delivery could have been completed by re-applying the extractor.

There were two failures when the head was in deep transverse arrest: in one case, traction alone would not overcome the difficulty, and when the rotator knob was used as an aid, the cup turned on the scalp; in the other case, the head did not budge. These patients were delivered by mid-forceps rotation and extraction, which required strong traction, and in both instances vaginal sulcus laceration occurred. In the 23 cases requiring rotation, the rotator knob on the suction cup was used to assist rotation in 10 cases, the others rotating spontaneously during the application of traction. One baby was extracted in the occipito-posterior position.

#### SUMMARY

The experience with the Malmström vacuum extractor reported here supports the conclusion that this instrument has a very useful, and probably a permanent, place in obstetrical practice. However, the conclusion of Pigeaud, who advocated the use of the extractor in all cases in order to shorten labour, does not seem to be justified, nor do we consider that

Evelbauer<sup>2</sup> is justified in citing failure with the vacuum extractor as an indication for Cesarean section. We have rotated and delivered babies with forceps in the present series after having failed with the vacuum extractor, and these were both cases of difficult rotation and extraction, in which vaginal sulcus lacerations occurred. Does this constitute good or bad obstetrics? Certainly, in the hands of the inexperienced operator, Cesarean section is to be preferred to traumatic mid-pelvic maneuvers with forceps. Our experience, like that of Tricomi, Amorosi and Gottschalk, justifies a more extensive trial of the vacuum extractor before difficult forceps maneuvers are attempted. We believe that a trial with the vacuum extractor in all such cases would result in a lowering in the frequency of forceps rotations.

In conclusion, because of its safety for both mother and child, the simplicity of its use, and its proved effectiveness, we recommend that the Malmström vacuum extractor become a part of the standard operating equipment in all delivery rooms.

We express our thanks to Dr. Evan MacCallum, Head of the Department of Obstetrics and Gynecology, for access to clinical material and for wise counsel, and to Drs. Oscar Nutik, Robert Greening and Claude Cronhelm for their devoted co-operation in this study.

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### CANADIAN JOURNAL OF SURGERY

Volume 4, No. 5 issue of the Canadian Journal of Surgery will be published in October 1961. Subscription rates to the Canadian Journal of Surgery are \$10.00 per year for four issues or \$2.50 for a single copy.

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*Experimental Surgery:* The etiology and pathogenesis of cholecystitis: an experimental study—D. J. Currie. Some observations on peripheral blood flow, blood gas, and electrolyte content of the dog's limb after sympathectomy—R. K. Padhi and R. B. Lynn. Splenic and bone marrow homografts in the dog after lethal body irradiation—J. W. Irvine and S. Kling.

# **PELIZAEUS-MERZBACHER'S DISEASE WITH SKELETAL MALFORMATIONS**

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PELIZAEUS-MERZBACHER'S disease is a rare disease of the central nervous system characterized by familial incidence, an onset in infancy with an extremely gradual and protracted course, and a combination of pyramidal, extrapyramidal and cerebellar signs.

The disease is transmitted by an apparently healthy mother and generally occurs in more than one member of a family. Males are predominantly affected, and a sex-linked recessive mode of transmission has been postulated. Nevertheless, an occasional case has been described among female members of affected families and its occurrence attributed to manifestations in the heterozygote, although the possibility that inheritance might be by an autosomal dominant gene with diminished penetrance in the female<sup>1</sup> has not been excluded. In any case, the severity of the disease has mostly been reduced when it has occurred in females.<sup>2</sup>

At one time regarded as a congenital aplasia of myelin sheaths—hence the synonym "aplasia axialis extracorticalis congenita"—it was later classified as a type of demyelination, and more recently has been assigned to the group of leukodystrophies where, in contrast to demyelinations of disseminated sclerosis and Schilder type, a congenital defect of enzyme activity is suspected. Seitelberger<sup>3</sup> regards Pelizaeus-Merzbacher's disease as a glycerophosphatide dystrophy of the myelin sheath because with appropriate methods it can be shown that the axons are covered by a thin layer of lipid material containing sphingomyelins and cerebrosides but no glycerophosphatides. Cummings<sup>4</sup> suggests that myelination may cease in the early years of life, later degeneration occurring in the myelin that has been formed. The axons themselves remain fairly well preserved. The pathological process is diffuse and symmetrical, involving the white matter of the cerebral hemispheres and basal ganglia and extending ultimately to brain-stem, cerebellum and spinal cord. An intense gliosis accompanies the slow spread of this process. A distinctive feature is the persistence within affected areas of small perivascular zones where the myelin is intact. The grey matter is generally unaffected.

After the first few years the course of the disease is so exceedingly slow that, although it commences in infancy, the patient's life may not be appreciably shortened. Genuine remissions may also occur. Its outstanding symptoms, as seen in the family first studied by Pelizaeus and later by Merzbacher,<sup>5</sup> are speech disturbance, bradylalia (slow and scanning speech), foolish grimacing facial expression,

ataxia, intention tremor, athetosis, choreiform movements, spasticity and mental deterioration. Some variations in the clinical syndrome have since been noted in the different families which have been reported. The general characteristics according to Merritt<sup>6</sup> are nystagmus, intention tremor, ataxia, spasticity, dysarthria and trophic disturbances. Buchanan<sup>7</sup> stresses the prominence of cerebellar signs as a distinctive characteristic.

The first signs commonly appear at about the age of three months; these are usually nystagmus, rotary movements of the head, and inability to sit up or support the head and back.<sup>8</sup> Some or all of the initial symptoms may partly or entirely disappear and be replaced later by others. However, the importance of ocular manifestations is underlined, both as an initial phenomenon and throughout the course of the disease. Ford<sup>9</sup> draws attention to the presence of rotary nystagmus at the onset. Merzbacher stresses nystagmus and twitches in the region of head and neck, and relates how, in the family observed by him, the old grandmother watched each new child for the telltale oscillations of the eyes. Buchanan<sup>7</sup> considers the most characteristic sign of the disease to be the bizarre movements which develop in the eyes. Occurring in central fixation, these are either rotary or lateral, much slower and wider in range than the jelly nystagmus sometimes seen in disseminated sclerosis, and so constant and irregular as to impede normal synchronous and conjugate movement. On lateral deviation of the eyes an ordinary horizontal nystagmus can frequently be elicited. The eyes may be further affected by primary optic atrophy.

These initial symptoms are generally followed by spastic weakness of the lower extremities, and this gradually extends until, years later, there is involvement of the upper extremities. At this stage the deep reflexes are increased, ankle clonus is present and plantar responses are extensor. However, in Scheftel's<sup>10</sup> cases abnormal reflexes, such as extensor plantar response, ankle clonus, and absent abdominals, were elicited only inconstantly. This author also stated that Pelizaeus noted inconstant clonus and intermittent tremor among his patients. Absence of deep reflexes has also been reported.<sup>11</sup>

Ataxia of cerebellar type appears subsequently, accompanied by intention tremor and scanning speech. Ataxia of the trunk develops and is associated with incoordination of the limbs and as the disease runs its slow course ataxia usually becomes much greater than spasticity. About this time, or even later, extrapyramidal symptoms make their appearance. Choreic, athetoid or other involuntary movements occur, or the picture becomes one of rigidity with immobile features and cog-wheel resistance in the extremities. Finally, weakness may give way to paralysis, and contractures develop with the production of scoliosis and pes cavus. Trophic changes in the bones of an osteoporotic and osteomalacic nature have been reported. The

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sphincters are not usually affected and sensibility is undisturbed.

Mental deterioration is a constant accompaniment. According to Merritt<sup>6</sup> deterioration of intellectual faculties is mild or moderate, although Penrose<sup>2</sup> mentions the occurrence of idiocy within the first decade of life. Like other features of the disease, mental deterioration may be equally slow in manifesting itself but it seems to be apparent generally by the age of six years. When the child reaches school age his intelligence may be found to be within the moron range. Over the years a very gradual decline in intellectual level occurs, and in extreme instances it may progress as far as idiocy. In other cases deterioration of intelligence appears to be arrested in childhood, and a further variation is seen in others in whom deterioration progresses at such an infinitesimally slow rate that the patient succeeds in retaining an intelligence within the moron or imbecile range.

#### CASE REPORT

The patient, the third eldest of eight children, was born in 1914. Her paternal grandparents were believed to have been well physically and mentally, but little was known of them. Of the maternal grandparents, the grandfather had been healthy up to the time of his death at the age of 77, apparently from cardiovascular degeneration; the maternal grandmother was still alive and well in 1931, at the age of 72. The patient's father and mother were born abroad; they were not related to each other. The father died with heart disease of an undefined nature at the age of 38 when the patient was 17 years old; the mother, aged 71, was known to be alive at the end of 1960. Of the patient's siblings, one brother died of an unknown cause at the age of six weeks. Another brother, eight years younger than the patient, was known to suffer from a slowly progressive neurological disorder. In 1931, when nine years old, he was described as physically and mentally weak; 30 years later he was apparently still able to get about, although said to be considerably handicapped by jerking movements of the head.

The patient was born precipitately at full term. She was breast fed and weaned at six months, and sitting up and walking were delayed. This girl did not begin to walk until she was fully three years old; she was considered to have a weak back and it was suspected that she had spinal trouble. Although she was uttering single words at the age of three years, it was several years later before she was forming sentences, and her speech was difficult to follow. The date of onset of abnormal movements of the eyes was not mentioned. Her relatives considered her mentally retarded from birth. Schooling commenced at the age of 11 years; by the age of 17 she had not progressed beyond Grade 2 and her right to a place in this grade even was dubious. At this time, 1931, she was admitted to the Manitoba School.

Examination on admission showed that she was a well-built girl in good general health. On examination of the skeletal system it was noted that both great toes were exceptionally broad with a raised vertical ridge along the mid-line. The patient was difficult to understand because of dysarthria. The deep reflexes were

increased and plantar responses were indeterminate. No unusual facial movements were noted, stance and gait were regarded as normal, co-ordination was unimpaired, and no abnormality was found in the sensory system. The most outstanding characteristic recorded was the presence of a constantly changing bilateral rotary nystagmus. An estimate of intelligence made with the Stanford-Binet scale gave her an I.Q. of 32, although the proviso was inserted that her rudimentary English vocabulary might have been partly responsible for an unduly low I.Q.

Fifteen years later, in 1946, she was active and in good general health. Bilateral rotary nystagmus and dysarthria were noted as before. Special mention was made of the weakness of the back although its nature was not specified. There was no recorded evidence of ataxia of the limbs, and judging from the fact that she was actively engaged in embroidery and was reported to be expert at knitting, it seemed clear that she had no difficulty in carrying out fine movements. However, during the course of the subsequent 15 years a gradual deterioration became apparent to those looking after her. Her movements became more awkward, her balance more easily upset, her gait more unsteady, and her face occasionally distorted by grimaces. The patient was capable ultimately of only relatively coarse work like washing floors. When examined in 1957, her most prominent symptom was ataxia, which was apparent in her stance, gait and during the performance of skilled voluntary movements. Muscle tone was also reduced; her deep reflexes did not show the exaggeration present earlier; the left abdominal reflex was diminished, and left plantar response was extensor.

When seen recently the patient was an undersized, obese woman, 4 ft. 11 in. in height and 165 lb. in weight. On examination of the nervous system, her fundi and fields of vision were normal, and visual acuity was about the same as at the previous examination. A slow rotary nystagmus was present on central fixation as well as on lateral gaze, and the involuntary movements were sufficiently pronounced to interfere with the normal synchronous and conjugate movements of the eyes. The peculiar quality which these constant movements gave the patient's appearance was enhanced by involuntary movements of the face in which the patient successively narrowed her eyelids, elevated an eyebrow, pursed her lips or carried out other movements. Her hearing was normal but her speech was indistinct with a tendency to scanning. The motor system showed considerable involvement, especially in the area of co-ordination. There was obvious truncal ataxia. Thus stance was unsteady and the patient tended to sway forward; she could not stand with her feet tandem (one behind the other) without losing her balance, and standing on one foot was only possible momentarily. With her arms crossed on the chest, she was quite unable to rise from a supine position; when sitting with her back unsupported, the swaying of the trunk and oscillations of the head were noticeably increased. Her gait was slow and tended to be shuffling, and walking tandem along a straight line was impossible. Closing the eyes made little appreciable difference to the ataxia. Limb ataxia was brought out by the finger-nose, finger-nose-finger, heel-knee and toe-finger tests. Errors were apparent in the range, force and direction of movement. Excessive rebound was present and an intention tremor was revealed. Performance of alternate movements such as pronation-



Fig. 1

supination and finger wiggling was also slow. Tone was about normal in the legs, but the muscles of the arms were soft and flabby and hypotonia was further apparent in hyperextension of the elbows. Involuntary movements were most obvious in the face, but occasional spasmodic jerking or tic-like movements occurred in the arms, and an involuntary shrugging of the shoulders was present; muscular atrophy and fibrillary twitching were absent. Deep reflexes, although reduced, could still be elicited; abdominal reflexes were more obviously reduced on the left side, and both plantar responses were extensor. There was no loss of



Fig. 2

sphincter control and sensation was undisturbed. Trophic disturbance was noticeable in the progressive alopecia which had thinned the hair over the anterior half of the scalp with the production of bald areas over which the remaining strands were stretched. The main feature of electroencephalographic examination was alpha activity of exceptionally low amplitude. An estimate of intelligence on the Stanford-Binet Scale yielded an I.Q. of 37. Considering that the original Binet I.Q. of 30 years ago had been suspected to be unduly low because of language difficulty, this latest I.Q. test quite possibly indicated that little or no further deterioration in intelligence had occurred.

In the skeletal system, the terminal lumbar vertebra was noted to be of transitional type and a small spina bifida of  $S_1$  was present. The fifth fingers of both hands were markedly incurved as in mongolism, and here also hypoplasia of the middle phalanges was found to be responsible (Fig. 1). However, the most striking anomaly was the excessively broad toes; radiographs revealed a state of polydactyly and syndactyly. There was duplication of distal phalanges, duplication and fusion of proximal phalanges, and a rudimentary additional metatarsal was present between the proximal extremities of first and second metatarsals (Fig. 2).

#### DISCUSSION

The patient reported here was one of two siblings with mental defect and protracted but slowly progressive neurological disorder; she showed pronounced delay in walking and talking, and speech was dysarthric once it was acquired. Intellectual retardation was present from a very early age. On admission to the Manitoba School at the age of 17 years the most obvious peculiarity was bilateral rotary nystagmus. Dysarthric speech and increased deep reflexes were other features recorded. During the period from 1931-1946 little change was noted in her state, but the weakness of the back mentioned in 1946 may possibly have heralded the onset of truncal ataxia. The subsequent 15 years witnessed a very slow deterioration which was reflected in her relegation to the performance of a coarser type of work than that which she had earlier been capable of doing. By that time her symptomatology consisted of rotary nystagmus, dysarthric speech, mild pyramidal and extrapyramidal signs, and quite marked cerebellar involvement with ataxia of trunk, incoordination of limbs and intention tremor. Despite the long duration of symptoms the patient appeared only moderately inconvenienced and was still ambulant and able to perform useful tasks. The familial history, the nature of the patient's symptoms, their very gradual development and protracted course suggested a diagnosis of Pelizaeus-Merzbacher's disease. The relative mildness of the clinical picture was also in keeping with the observed course of the disease when it occurs in females.

The differential diagnosis of Pelizaeus-Merzbacher's disease involves consideration of disseminated sclerosis, Schilder's diffuse sclerosis, and a number of less common progressive degenerative

conditions. Disseminated sclerosis is distinguished by such features as its later age of onset, more rapid progress, nature of ocular manifestations, and frequent sensory and sphincter involvement. The ordinary form of Schilder's diffuse sclerosis does not need to be considered, but the transitional form may present difficulty. Poser<sup>12</sup> has pointed out that transitional or diffuse-disseminated sclerosis may commence in childhood and run a prolonged course with an extreme range of 45 years. However, cortical blindness, convulsions, psychic disturbances apart from dementia, and various types of aphasia and apraxia are likely to occur. In congenital cerebellar ataxia, such features as mental defect, spasticity and athetosis may accompany ataxia, but the latter is obvious in infancy and the disease has no familial incidence. A familial type of cerebellar ataxia associated with mental defect has been described;<sup>13</sup> no other symptoms appear to occur. Mental defect and cerebellar ataxia also occur on a familial basis along with optic atrophy in Behr's syndrome,<sup>14</sup> with cataract in Marinescu-Sjögren syndrome,<sup>15</sup> and with telangiectasia in Louis-Bar's syndrome,<sup>16</sup> but in these conditions the associated features and general course are likely to be sufficiently distinctive for diagnosis.

The skeletal anomalies associated with Pelizaeus-Merzbacher's disease are osteoporosis and osteomalacia; polydactyly and malformation of phalanges have not previously been reported. Supernumerary digits occur as an isolated peculiarity in familial polydactyly; affected individuals are otherwise normal and most pedigrees show dominant inheritance.<sup>17</sup> Polydactyly of recessive type has been reported in association with ringed hair and melanoderma,<sup>18</sup> as well as with a number of other abnormalities of the skin. Polydactyly is associated with further skeletal abnormalities in chondroectodermal dysplasia, or Ellis van Creveld syndrome. Chondrodysplasia and shortening of tubular bones accompany dysplasia of hair, teeth and nails; but the polydactyly is generally limited to the hands and its occurrence in the feet is exceptional.<sup>19</sup> In the Lawrence-Moon-Biedl-Bardet syndrome, polydactyly accompanies mental defect, retinitis pigmentosa, obesity and hypogonadism. An ataxic gait has occasionally been noted in this condition,<sup>20</sup> and a connection with the hereditary ataxias has been suggested.<sup>21</sup> Poser, Dewulf and van Bogaert<sup>22</sup> have in turn suggested a link between the latter and the group to which Pelizaeus-Merzbacher's disease belongs, the leukodystrophies. Since transitional forms are known to occur between the clinically different heredo-degenerative diseases, it is possible that the polydactyly, obesity and reduced stature in the present case provide a link with the Lawrence-Moon-Biedl-Bardet syndrome.

However, reduced stature is the rule, obesity is frequent, and polydactyly and syndactyly of toes<sup>23</sup> have occasionally been observed in mongolism; where, incidentally, myelination in the brain is retarded in infancy, and later demyelination can

occur. The little fingers are also abnormal in mongolism. Hypoplasia of the middle and distal phalanges of the little fingers is said to occur in 1% of normal children,<sup>24</sup> but hypoplasia limited to the middle phalanges of the little fingers is a characteristic finding in mongolism, where it accounts for the marked incurving of these digits. According to Benda,<sup>25</sup> some degree of anomaly is present in the middle phalanges of the fifth digits in almost 90% of mongol defectives, and in about 60% of cases hypoplasia is sufficiently marked to produce the characteristic curvature. This peculiarity is particularly obvious in the present case and the skeletal anomalies might be interpreted as a link with mongolism.

#### SUMMARY

A case has been described presenting features characteristic of Pelizaeus-Merzbacher's disease. An unusual association is the occurrence of polydactyly along with hypoplasia of the middle phalanges of the little fingers. The question of a possible linkage between this case and Lawrence-Moon-Biedl-Bardet syndrome or with mongolism has been broached.

I am indebted to Dr. H. S. Atkinson, Medical Superintendent of the Manitoba School, for permission to make use of institutional records.

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## THE MYELOPROLIFERATIVE DISORDERS WITH SPECIAL REFERENCE TO HISTOCHEMICAL FEATURES\*

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THE myeloproliferative disorders constitute a group of primary diseases of the blood-forming tissues, characterized by abnormal, self-perpetuating proliferation of one or more of the bone marrow elements.<sup>1</sup> The marrow proliferation may be benign or malignant. Benign proliferation, such as the granulocytic response to infection, or a total marrow response to acute blood loss, are reversible. Malignant proliferations are irreversible.

Our studies concern the following irreversible myeloproliferative disorders: polycythemia vera, myelofibrosis, chronic granulocytic leukemia, thrombocythemia and megakaryocytic leukemia.

Polycythemia vera is characterised by erythrocytosis and, frequently, by a neutrophilic leukocytosis and thrombocytosis. The bone marrow shows a general hyperplasia of all the cellular elements, and very little fat is present. After a variable period of time there is a shift in the granulocytes towards immaturity, and many myelocytes and nucleated red cells may appear in the blood. If it is present, splenomegaly increases because of myeloid metaplasia, and a variable degree of fibrosis appears in the marrow; but occasionally the myeloid metaplasia of the spleen precedes the appearance of fibrosis in the marrow. Although it has been suggested that the myeloid metaplasia may appear in compensation to the marrow fibrosis,<sup>2</sup> it appears more likely that the same disease process affects all of the hematopoietic tissues simultaneously.

Although myelofibrosis may be preceded by polycythemia vera, the majority of cases occur independently. These patients usually have very large spleens. Anemia is frequent and becomes worse as the disease progresses; there are many tear-drop shaped red cells and normoblasts. There are variable numbers of white blood cells with occasional myeloblasts, a number of myelocytes and metamyelocytes. The platelets vary in number; they are reduced rarely except in the late stages, and many bizarre forms appear. Megakaryocytes are occasionally present. Because of such clinical and peripheral blood findings, this condition has been confused with chronic granulocytic leukemia. The bone marrow findings, however, are more characteristic. The cortex of the bone is usually hard; it is difficult to penetrate with the needle and diluted specimens are aspirated, occa-

sionally showing masses of platelets and some megakaryocytes. Marrow sections reveal a variable degree of fibrosis. The splenic enlargement is due to myeloid metaplasia which can be demonstrated on splenic aspiration.

In chronic granulocytic leukemia the anemia is usually more severe than in myelofibrosis but the morphologic changes of the red blood cells are less marked. The changes in the leukocytes and the degree of leukocytosis are usually more pronounced. The bone marrow is characteristically hypercellular because of an increase in the neutrophilic series, and the platelets and megakaryocytes are often increased.

Thrombocythemia is characterized by a profound increase in platelets, usually of bizarre forms; there is hyperplasia of the megakaryocytes in the marrow, although these precursors are morphologically normal. Despite the high platelet counts, these patients have a bleeding tendency. Thrombocythemia may be idiopathic or it may appear after splenectomy, but it is occasionally seen in patients with polycythemia vera or chronic granulocytic leukemia. Despite the widespread fibrosis of the marrow which occurs in myelofibrosis, the megakaryocytes are usually well preserved or increased, in contrast to the red cell and white cell precursors. However, the increase in platelets rarely reaches the level of the many million seen in thrombocythemia.

Megakaryocytic leukemia is a more controversial disorder. Since the megakaryocytes in the marrow are usually well preserved or increased in myelofibrosis, one of the many synonyms for this disorder is aleukemic megakaryocytic myelosis.<sup>3</sup> In myelofibrosis the megakaryocytes are usually normal in appearance. In our case there was a profound increase in number of abnormal bizarre megakaryocytes in the marrow. Similar cells were seen in material obtained on splenic aspiration. The platelets in the blood were normal in number but varied in size, shape and staining qualities. The platelets generally appeared larger than normal.

### HISTOCHEMICAL STUDIES

Chemical and cytological investigations have indicated differences in the alkaline phosphatase concentrations in the neutrophils of patients with infections, polycythemia vera, myelofibrosis and granulocytic leukemia.<sup>4-8</sup> These differences in the neutrophil alkaline phosphatase content in the various disorders of the myeloproliferative diseases have important diagnostic and theoretical implications.

### MATERIALS AND METHODS

The subjects studied were ward patients or patients seen in the hematology clinic of the Montreal Jewish General Hospital, and included five cases of polycythemia vera, four of myelofibrosis, three of chronic granulocytic leukemia, one of megakaryocytic leukemia, one of thrombocythemia

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and three of acute infection. There was a miscellaneous group which contained seven subjects with diseases such as lymphocytic leukemia, lymphosarcoma and idiopathic thrombocytopenic purpura. The 14 normal controls were selected at random from among members of the staff of the hospital who were free of any hematologic disorder or infection.

Peripheral blood smears were stained by the azo dye coupling method of Kaplow.<sup>9</sup> By this method the alkaline phosphatase activity in the cytoplasm of mature neutrophils is demonstrated by the presence of brown deposits (Fig. 1). The neutrophils

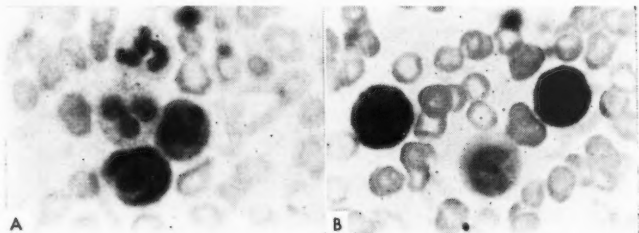


Fig. 1A.—Top: 0. Left centre: 1+. Right centre: 2+. Bottom: 4+. Fig. 1B.—Left: 3+. Right: 4+. Centre: 2+.

are graded from 0 to 4 plus, according to the intensity of the brown stain. One hundred consecutive neutrophils are graded in this way and the sum of the grades, usually referred to as the "score", reflects the alkaline phosphatase activity of the neutrophils. Two or more such scores were determined in each case.

RESULTS

**Controls**—The control alkaline phosphatase scores ranged from 7 to 120 with a mean of 52. Scores in the miscellaneous group ranged from 17 to 101 with a mean of 40. These findings are essentially similar to the control group. Fig. 2 presents these findings in graphic form.

**Acute infection**—Patients with acute infections had high alkaline phosphatase scores, ranging from 154 to 288, averaging 171.

**Polycythemia vera**—All of these patients had high scores, which ranged from 132 to 281, with a mean of 212.

**Myelofibrosis**—Two patients had high scores (158 and 207) and in the other two the scores were low (12 and 58). The patient who had a score of 207 originally, subsequently had a score of 35 three weeks later; and 49, five weeks later.

**Thrombocythemia**—The patient with thrombocythemia had a score of 175 when the platelet count was 3,000,000 per c.mm. After treatment with radioactive phosphorus, the platelet count dropped to 400,000, and the alkaline phosphatase score fell to 57.

**Megakaryocytic leukemia**—The patient with megakaryocytic leukemia had a score of 267.

**Chronic granulocytic leukemia**—All of the patients with chronic granulocytic leukemia had low scores which ranged from 4 to 42 and averaged 23.

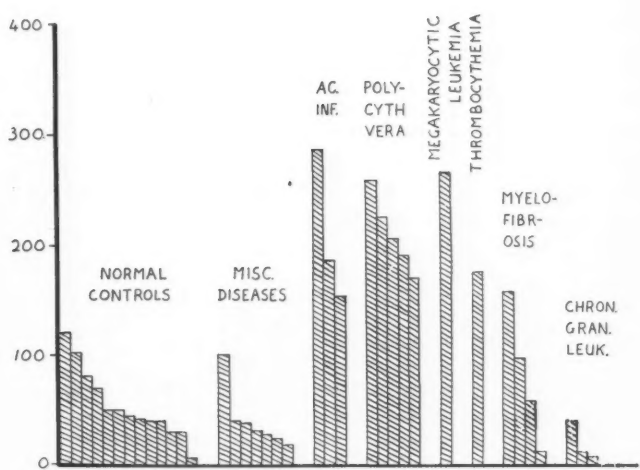


Fig. 2.—Alkaline phosphatase scores in controls and cases studied.

DISCUSSION

The findings of increased neutrophil alkaline phosphatase activity in polycythemia vera, acute infections, and in some cases of myelofibrosis, and of low alkaline phosphatase levels in chronic granulocytic leukemia are similar to those previously reported<sup>4-8</sup> (Table I). The high score in the

TABLE I.—COMPARISON OF ALKALINE PHOSPHATASE SCORES REPORTED BY DIFFERENT AUTHORS

	Present authors	Kaplow	Koler et al.	Mitus and Dameshek
Controls.....	52	22	73	30
Miscellaneous diseases.....	40	43	—	—
Acute infections....	209	237	156	—
Polycythemia vera..	212	189	170	205
Myelofibrosis.....	76	—	119	78
Chronic granulocytic leukemia.....	23	—	8	0.8
Thrombocythemia..	175	—	218	—
Megakaryocytic leukemia.....	267	—	—	—

patient with thrombocythemia is in the same range as that in the two cases reported by Koler *et al.*<sup>8</sup> Patients with myelofibrosis appear to fall into two groups: one with high scores and the other with low scores. This was also observed by Mitus *et al.*<sup>7</sup> and Koler *et al.*<sup>8</sup>

Myelofibrosis is an entity which appears to lie at the hub of the myeloproliferative disorders; it has been a controversial and poorly defined disorder for many years.<sup>10-13</sup> It has frequently been confused with chronic granulocytic leukemia because it has many features similar to this disease. Similarly, the impression that polycythemia vera frequently terminates as chronic granulocytic leukemia has not been borne out by alkaline phosphatase studies.<sup>14</sup> Actually, the transformation of polycythemia vera is usually toward myelofibrosis, in which the neutrophil alkaline phosphatase is high; it is only in its transition to acute leukemia that low alkaline phosphatase scores are found.<sup>14</sup>

Although the majority of patients with myelofibrosis have high alkaline phosphatase levels, and thus may be readily distinguished from those with chronic granulocytic leukemia, a significant number of patients have normal or low levels. In one of our patients who had clinical and hematological features suggestive of leukemic transition, the alkaline phosphatase was low. In another patient who did not have evidence of clinical disease other than a slowly progressive anemia, the alkaline phosphatase activity changed from a high to a low value during observation. Low alkaline phosphatase activity presaged the development of leukemia in atomic bomb casualties in Japan;<sup>15</sup> similarly this may suggest that low alkaline phosphatase in patients with myelofibrosis may herald conversion to a leukemic phase.

One of the most interesting conclusions which comes from the alkaline phosphatase studies is that morphologically identical cells may be different metabolically; and that the low alkaline phosphatase cells of chronic granulocytic leukemia may represent a different cell lineage from the normal cell.<sup>14</sup>

The diagnostic significance of the leukocyte alkaline phosphatase enzyme is most evident in chronic granulocytic leukemia. Low values in this condition have been so well documented that one hesitates before making such a diagnosis in the presence of normal or high values.<sup>16</sup> This test is also of value in distinguishing a leukemoid reaction, which shows a characteristically high score, and most cases of myelofibrosis, from chronic granulocytic leukemia. Moreover, polycythemia vera may also be distinguished from secondary polycythemia by the normal alkaline phosphatase scores in the latter condition.<sup>17</sup>

It is difficult to establish at the present time whether the different conditions included in the myeloproliferative disorders represent varied aspects of the same fundamental process;<sup>10, 11</sup> or whether they are similar morphologic expressions of different etiologies. The variations in the neutrophil alkaline phosphatase content of this group of diseases supports the latter hypothesis. In addition, the usually distinct clinical and hematological features and the different prognoses,

managements and responses to therapy readily differentiate the conditions from one another. Difficulties in differential diagnosis are actually uncommon, although transitional forms and transformations do occur. However, the not infrequent history of leukemia or lymphoma in a member of the family of a patient with myelofibrosis is in favour of a closer etiologic relationship of these disorders. This association was found in two of our patients. However, in the final analysis disease results from a combination of environmental factors and the subsequent reaction of the body and its tissues to these factors. Thus, whether in response to one or more stimuli the primitive reticulum cell may differentiate in varying degrees into megakaryocytes, erythroblasts, leukocytes or fibroblasts, the end result of this interaction appears to lead to a specific disorder. The term myeloproliferative disorders refers to the group of conditions with similar morphologic features but without implying any common etiology.

#### SUMMARY

Some of the diseases included in the myeloproliferative disorders have been discussed. Neutrophil alkaline phosphatase scores were determined in patients with these diseases as well as in controls. High scores were found in patients with infection, polycythemia vera, thrombocythemia and megakaryocytic leukemia. Patients with myelofibrosis had both high and low scores. In chronic granulocytic leukemia the scores were low.

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#### PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

"One of the most interesting discoveries is that of Zuelzer, Dohrn and Marxer that the mucous membrane of the stomach contains a hormon, which when injected intravenously was found to stimulate intestinal peristalsis. It was later demonstrated that the same hormon can be extracted from the spleen in amounts sufficient to enable it to be utilized therapeutically. This discovery is of interest both to the physician and surgeon in the treatment of intestinal obstruction from atony of the bowel, as well as of postoperative intestinal paralysis. The results reported by Zuelzer and Saar with hormonal, the name under which

this hormon product has been introduced, have been most encouraging. Its advantage over physostigmin, which has been employed for the same purpose, is that it produces a natural peristalsis and not one of tetanic character. While symptoms of reaction, such as fever and headache, have been noted from its use, these have been of slight and transient nature, and there is every reason to believe that this new physiologic product will prove of material service in medical and surgical practice."—*International Journal of Surgery*; quoted in *Canad. M. A. J.*, 1: 936, 1911.

## LA REDUCTION DE LA MASSE CEREBRALE DANS LE TRAITEMENT DE L'ÉPILEPSIE INCONTROLABLE NON FOCALISEE\*

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L'IMPOSSIBILITÉ de réduire la fréquence des crises épileptiques par l'emploi varié de toutes les médications anticonvulsivantes présente un sérieux problème aux cliniciens neurologues. Certains malades en arrivent même à présenter une complication plus grave encore: l'état de mal ou status epilepticus incontrôlable par des mesures thérapeutiques médicales élaborées telles que l'oxygénothérapie, l'anesthésie générale ou l'hypothermie. Nous avons déjà été confrontés avec ce problème et dans quelques cas nous avons dû recourir, en désespoir de cause, à une tentative thérapeutique chirurgicale. Il s'agissait de malades souffrant d'épilepsie d'origine cérébrale non focalisée, parvenus au stade incontrôlable par la médication ou à l'état de mal épileptique où le malade, déjà hospitalisé, devait être gardé sous une surveillance étroite.

Par épilepsie non focalisée, nous entendons l'état morbide dans lequel l'examen électro-encéphalographique n'a pas réussi à mettre en évidence indiscutable un foyer cérébral cortical épileptogénique bien localisé et constant. L'origine des décharges électriques est donc imprécise; elles semblent venir des structures sous-corticales ou centrencéphaliques avec projections secondaires au cortex. Dans d'autres cas, les décharges avaient comme point de départ des ondes multifocales accompagnées d'anomalies diffuses dans le tracé de base, auxquelles se surajoutant des décharges épileptiformes migratrices d'une région à l'autre du cortex.

L'observation des résultats opératoires chez des malades atteints de paralysie cérébrale nous a permis d'émettre une hypothèse qui a servi de fondement à notre tentative thérapeutique chirurgicale.

Dans la paralysie cérébrale infantile où l'atrophie cérébrale prédomine dans un hémisphère, il existe des cas où sont associés: hémiplégie, hémiconvulsions, troubles caractériels et mentaux. Ford<sup>1</sup> classifie cette maladie en distinguant l'hémiplégie infantile aiguë ou encéphalite, de l'hémiplégie congénitale dont l'étiologie est obscure mais souvent attribuée à un traumatisme de la naissance. En 1950, Krynauw<sup>2</sup> présente douze cas d'hémisphérectomie pour hémiplégie infantile avec hémiatrophie corticale. Dans tous les cas, l'hémiplégie en soi n'était pas une indication suffisante pour la

chirurgie. Les convulsions et les troubles mentaux importants devaient constituer la triade. Laine et Gross,<sup>3</sup> dans une excellente monographie sur "l'Hémisphérectomie" rapportent 39 observations; 30 de ces malades souffraient d'encéphalopathies infantiles. Les résultats consécutifs à l'exérèse d'un hémisphère pathologique sont les suivants: disparition des crises d'épilepsie, amélioration des troubles caractériels et mentaux, apparition de l'attention et de la mémoire, amélioration de la motricité par diminution de la contracture pyramidale, amélioration de l'état général, augmentation de l'appétit et du poids, autant de facteurs qui rendent désormais possible l'éducation dans le milieu familial. A peu près les mêmes conclusions peuvent être tirées de l'observation des cas d'hémisphérectomie que nous avons traités à l'hôpital Ste-Justine.

La disparition des crises d'épilepsie après l'opération est le fait particulier qui a retenu notre attention chez les hémisphérectomisés. Plusieurs de ces malades présentaient des signes d'activité épileptique aux deux hémisphères; après l'exérèse de l'hémisphère malade, l'hémisphère restant redevenait normal du point de vue E.E.G. Ce fait a été constaté aussi par Obrador.<sup>4</sup> Après l'exérèse d'un hémisphère atrophique chez une adolescente de 17 ans, les crises convulsives ont cessé et les anomalies électro-encéphalographiques ont disparu dans l'hémisphère opposé. Il nous a paru que l'hémisphérectomie dans ces cas avait un double effet à l'égard de l'épilepsie: d'une part, l'exérèse du foyer pathologique épileptogène, d'autre part, la réduction opératoire de la masse totale du cerveau où pratiquement la moitié a été enlevée. Cette exérèse a réduit également les connections des grandes voies associatives distribuées dans l'hémisphère controlatéral. Ce qui pourrait expliquer aussi la disparition de l'activité épileptique secondaire de l'autre hémisphère après l'exérèse de l'hémisphère pathologique.

Nous avons eu l'occasion d'observer des cas d'encéphalopathie corticale diffuse associée cliniquement à de l'épilepsie dont le point de départ est imprécis et inconstant, non latéralisé et non focalisé. A un moment de l'évolution, la fréquence des crises est devenue incontrôlable par toute médication anti-convulsivante. Quelques malades ont présenté en plus la complication la plus sérieuse d'un état de mal réfractaire à l'oxygénothérapie, aux neuroleptiques à hautes doses et à l'hibernation artificielle. Vu l'impossibilité de mettre en évidence un foyer cortical bien localisé, toute exérèse chirurgicale élective est impossible. Nous avons alors tenté de soumettre le malade à une intervention chirurgicale *non élective* dont le fondement physiopathologique nous a paru empirique, mais inspiré du moins de l'observation des résultats post-opératoires des cas d'hémisphérectomie dont nous avons parlé plus haut. Nous avons pratiqué l'exérèse d'un lobe pré-frontal afin de réduire la masse cérébrale. Le choix du lobe pré-frontal n'était pas déterminé par l'état électroencéphalographique ou clinique du patient.

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Tout autre lobe aurait pu être enlevé théoriquement, mais nous ne l'avons pas fait à cause des fonctions importantes attribuées aux lobes temporal, occipital et pariétal chez l'humain. Seul, le lobe pré-frontal est cliniquement silencieux du point de vue neurologique. Et chaque fois, le lobe gauche ou droit a été choisi non pas en vertu des modifications électriques du tracé, mais suivant la prédominance hémisphérique du patient droitier ou gaucher. A cette époque nous n'étions pas familiers avec l'épreuve de l'injection intracarotidienne d'amytal sodique dans le but de latéraliser le centre de la parole.

#### PREMIERE OBSERVATION

Cet enfant de six ans et demi est suivi depuis 1952, dans le service de neurologie de l'hôpital Ste-Justine, pour débilité mentale et crises épileptiques qui ont débuté vers l'âge de quatre mois. Il faisait jusqu'à 10 crises de grand-mal par jour, lesquelles étaient partiellement contrôlées par la médication. Depuis trois mois, malgré les essais variés de médicaments, les crises sont plus rapprochées et plus intenses, il fait jusqu'à 40 crises de grand-mal par jour. La pneumoencéphalographie montre une atrophie corticale marquée aux régions frontale et pariétale gauches. L'électroencéphalogramme montre des anomalies diffuses et plus prononcées dans les régions antérieures, suggérant une atteinte corticale généralisée.<sup>1</sup> Aucune activité épileptique franchement latéralisée est observée. A cause de l'état clinique incontrôlable du patient, on pratique une lobectomie frontale droite le 14 mai 1956. Le lobe frontal droit a été choisi parce que le patient est droitier, en supposant que l'hémisphère gauche est dominant. A l'exploration, le cortex cérébral était atrophique et l'examen histo-pathologique du fragment tissulaire montrait qu'il y avait de la fibrose cérébrale diffuse. Les suites post-opératoires furent sans incident sauf que le patient a fait une crise d'épilepsie le lendemain de l'opération. Il n'en a plus fait depuis. L'E.E.G., un mois plus tard montre une amélioration par rapport au premier tracé bien qu'il persiste encore des anomalies légères dans les régions antérieures de l'hémisphère gauche. Aucune activité épileptique n'est notée. Le malade a quitté l'hôpital avec une médication de 1½ grains de Dilantin (100 mg diphénylhydantoïne) matin et soir qui suffit à contrôler ses crises. Un an plus tard, il eut une infection rénale grave qui laissa des séquelles de néphrite chronique amenant la mort en janvier 1961. Il n'avait plus jamais fait de convulsions généralisées. On rapporte qu'au stade terminal dans les mois qui avaient précédé sa mort, il avait recommencé à faire des absences quotidiennes.

Certains cas d'épilepsie centrencéphalique (dite essentielle ou idiopathique, sans lésion organique décelable) s'accompagnent souvent de troubles caractériels et mentaux importants. D'après la conception de Reynolds:<sup>5</sup> "Seule cette forme de convulsions idiopathiques mérite le nom d'épilepsie proprement dite, car il s'agit d'une *perturbation fonctionnelle* du cerveau, d'un déséquilibre des systèmes régulateurs centrencéphaliques. Toutes les autres formes d'épilepsie ne sont que des manifestations cliniques d'autres maladies ou d'une

lésion organique cérébrale, auxquelles le terme d'épilepsie ne s'applique pas à proprement parler."

Nous avons aussi appliqué cette méthode ligne de conduite dans les cas d'épilepsie centrencéphalique parvenus au stade incontrôlable.

#### DEUXIEME OBSERVATION

A sept ans, cet enfant présente des crises convulsives depuis l'âge de 4 ans et pour lesquelles il a reçu une médication anticonvulsivante soutenue. Cependant, les crises se répètent à la fréquence de deux crises de grand-mal chaque nuit et, durant le jour, il fait de très nombreuses crises de petit-mal. L'électroencéphalogramme montre des anomalies diffuses avec des décharges épileptiques d'origine centrencéphalique aussi bien que corticale. Le pneumoencéphalogramme révèle une atrophie cérébrale diffuse et surtout manifeste au lobe temporal droit. Le 20 septembre 1957, on pratique une lobectomie pré-frontale. Comme le malade est ambidextre, le lobe pré-frontal gauche est enlevé. Les suites post-opératoires sont sans incident.

Durant les mois qui ont suivi, le patient a fait trois crises de grand-mal survenant surtout la nuit, durant le sommeil. Les crises de petit-mal sont beaucoup diminuées; elles se manifestent par de petites absences très brèves qui durent à peine une fraction de seconde. Par ailleurs, le comportement mental de l'enfant s'est beaucoup amélioré, il est plus sociable et, selon les parents, plus facile à éduquer. Il a tout de même de la difficulté à étudier ses leçons et à les réciter le lendemain. Cette difficulté semble en rapport surtout avec la difficulté de fixer son attention et elle se manifeste par son caractère versatile au cours de la conversation. Par la suite, les crises convulsives ont diminué de fréquence en survenant aux 15 jours, puis enfin une fois par mois. Un an plus tard l'électroencéphalogramme montre une grande amélioration du tracé. Il n'y a aucune décharge de pointes-ondes ni au repos, ni à l'hyperventilation, ni à la stimulation lumineuse intermittente. Au mois de septembre 1958, l'enfant est retourné à la classe et ses parents constatèrent une amélioration notable de la mémoire et de ses facultés intellectuelles. L'enfant n'a pas fait de crises depuis six mois. Durant le premier mois de l'année scolaire, il réussit sans fatigue à assimiler la matière de ses études. Au point de vue de son caractère et de son comportement, la mère est très heureuse et elle ne se plaint d'aucune difficulté à l'éduquer. A la fin de l'année scolaire en 1959, l'enfant a fait une année de classe régulière et il a bien réussi dans ses études au point qu'il est qualifié pour entreprendre sa 2e année en septembre prochain. Un psychologue a conseillé d'envoyer l'enfant à une école régulière avec les autres enfants. La médication anticonvulsivante assure un contrôle parfait des crises. Il ne reçoit que ¼ de grain (45 mg) de Dilantin le matin et le soir, et 5 mg de Dexédrine (sulfate d'amphétamine) au coucher occasionnellement.

#### TROISIEME OBSERVATION

Un adolescent de 18 ans fait des crises d'épilepsie de grand mal depuis l'âge de huit ans, survenant par bouffées de trois ou quatre crises par jour durant trois à quatre jours de suite par semaine. Il est aussi en proie à des accès de rage qui ont été interprétés comme des manifestations de "sham rage" au cours

desquelles il entre dans une colère irrésistible cassant tous les objets à portée de sa main et frappant les gens qui l'entourent. Ces accès de rage précèdent parfois les crises et se terminent toujours par une crise de grand-mal. On note dans ses antécédents qu'il a fait une rougeole, une otite chronique et des maux de gorge à répétition. En 1943 il avait subi une fracture du crâne, pour laquelle il avait été suivi longtemps pour prétendue épilepsie post-traumatique. L'examen général et l'examen neurologique ne montrent rien de particulier. Le pneumoencéphalogramme révèle une atrophie cérébrale diffuse plus marquée à l'hémisphère gauche avec adhérences cortico-méningées. L'électroencéphalogramme témoigne d'une pathologie diffuse corticale et sous-corticale avec activité épileptique dans la région temporale droite de même que des décharges épileptiques d'origine centrencéphalique. Toutes les médications anticonvulsivantes ont été essayées mais sans effet sur la fréquence et l'intensité des crises. Il a reçu en plus, de l'oxygénothérapie et des neuroleptiques à hautes doses. Devant l'impossibilité de contrôler ses crises, nous avons d'abord tenté une lobotomie médicale du lobe frontal droit, par injection de Novocaïne (procaïne). Quelques heures après l'intervention il a fait une crise convulsive qui a duré cinq minutes et il n'a pas fait de crise ensuite durant quatre jours. Le Largactyl (chlorpromazine) ajouté à la médication assure un comportement meilleur, l'enfant étant plus calme et plus tranquille. Mais les crises de grand-mal sont réapparues de sorte que nous décidons de pratiquer l'exérèse du lobe pré-frontal droit. Les études histopathologiques montrent une substance cérébrale d'aspect normal sauf qu'à un endroit elle contenait une plaque hémorragique due à l'injection de procaïne faite auparavant. La médication anticonvulsivante est continuée et le patient continue encore à présenter des crises convulsives, mais l'intensité est moins grande et la périodicité beaucoup plus longue. Il est parfois 15 jours sans faire de convulsions. Par ailleurs, les crises dites de rage ont complètement cessé. L'enfant est plus sociable et son comportement mental est meilleur. Il reçoit continuellement une médication au Dilantin et au phénobarbital.

#### QUATRIÈME OBSERVATION

Cette malade de 22 ans est traitée depuis six ans pour des crises épileptiques se manifestant surtout par du petit-mal, alternant avec des crises de grand-mal survenant trois ou quatre fois par jour. La malade affiche aussi un comportement mental extrêmement difficile et un état d'insubordination à tel point qu'elle est devenue insupportable pour son entourage. Toutes les médications anticonvulsivantes ont été tentées sans pouvoir diminuer la fréquence et l'intensité des crises. L'électroencéphalogramme est typique d'un processus épileptique d'origine centrencéphalique du genre petit-mal grand mal. On pratique une lobectomie frontale droite. Depuis l'intervention, la médication anticonvulsivante habituelle suffit à contrôler les crises. Par la suite la patiente s'est mariée et a eu un enfant. Selon son mari, la malade peut passer de grandes périodes sans manifester de troubles du caractère. Cependant, étant d'un naturel plutôt négligeant, elle oublie pendant plusieurs semaines de prendre sa médication anticonvulsivante et alors les crises convulsives réapparaissent. Mais dès que la médication au Dilantin et au phénobarbital est reprise les crises sont bien

contrôlées. Pourtant, un E.E.G. pratiqué un an après l'intervention montre encore la présence d'un processus épileptique d'emblée généralisé et d'origine centrencéphalique mais avec prédominance des décharges dans l'hémisphère droit.

#### COMMENTAIRES

Nous avons à l'heure actuelle trop peu de cas et trop peu de recul dans le temps (cinq ans) pour établir la valeur de cette conduite thérapeutique, mais dans les cas où l'amélioration a été importante, on peut dire que les malades ont tiré un certain bénéfice de cette conduite.

Cependant, nous sommes loin de comprendre le mécanisme qui a produit ces résultats. Nous avons l'impression que les grands efforts de l'épileptologie moderne ont été accomplis surtout dans le but de préciser et de définir la nature, le comportement biochimique et les modifications physiopathologiques de la lésion épileptogénique focale. La science expérimentale a fourni des renseignements très précieux sur ce qui se passe dans les neurones à partir du moment où ils déchargent de façon paroxystique. Mais il y a lieu de se demander si on a peut-être confiné cette recherche au microcosme de la cellule nerveuse au dépend du macrocosme du reste de la masse cérébrale. A l'heure actuelle on ne sait à peu près rien de ce qui se passe ailleurs, dans le cerveau simultanément ou avant qu'une région précise devienne la source de décharges paroxystiques. Qu'est-ce qui fait qu'une lésion épileptogène n'est pas continuellement en activité mais qu'elle ne se manifeste que périodiquement, bien qu'anatomiquement il n'y ait pas de modification structurale? N'y aurait-il pas un paramètre tout à fait indépendant de la lésion épileptogénique et qui conditionnerait à l'occasion ou périodiquement sa réactivation électrique? En l'occurrence, le substratum de la masse cérébrale entière aurait-il dans sa totalité une physiologie de masse, un comportement volumétrique irréductible aux fonctions différentielles des lobes, des centres, des zones, des circonvolutions ou des noyaux? La physiologie de la masse cérébrale comme unité d'étude ne nous semble pas encore démontrée, mais nous avons l'impression qu'il y a une source de renseignements qui seraient très utiles au sujet de la dynamique cérébrale. Amantea et Baglioni<sup>6</sup> ont déjà mentionné, à propos d'expériences sur l'épilepsie réflexe, qu'un pourcentage notable de chiens s'y révèle réfractaire. Il existe donc des sujets prédisposés et d'autres non prédisposés à l'épilepsie réflexe. Ce problème de la prédisposition à l'épilepsie est un fait cliniquement démontré puisqu'un faible pourcentage seulement de traumatismes crâniens (2.5%) est suivi d'épilepsie Jacksonienne ou d'épilepsie généralisée. Il semble y avoir des conditions particulières à l'apparition d'une crise d'épilepsie. Ces conditions ne dépendent pas du foyer initial ou de la lésion épileptogénique, mais du substratum entier de la masse cérébrale dont les modifications possibles de

la dynamique sont susceptibles d'influencer secondairement le foyer épileptogène. Penfield et Jasper<sup>7</sup> avaient déjà observé que l'application locale de strychnine ne pouvait amener régulièrement des convulsions généralisées chez tous les animaux, mais seulement chez des sujets "susceptibles". Les convulsions généralisées se produisaient seulement lorsque la strychnine était administrée par voie intra-veineuse ou qu'elle avait diffusé dans le flot sanguin par suite d'une application locale prolongée. Ceci suggère que d'autres mécanismes entrent en jeu pour transformer l'activité d'un foyer potentiellement épileptogène en une crise convulsive généralisée. Soit que l'activité du foyer soit grandement augmentée, ou soit que le reste du cerveau devienne momentanément plus susceptible ou "prédisposé" à la décharge épileptogène focale. Nous avons l'impression qu'il existe une physiologie de la masse cérébrale, mais que cette notion est encore imprécise du point de vue neurophysiologique. Elle pourrait être illustrée par l'analogie suivante: du point de vue fonctionnel, le cerveau entier ou la masse cérébrale se comporterait comme un condensateur. Dans une première phase, il accumule des charges électriques et emmagasine de l'énergie. Dans une deuxième phase, il se comporterait comme un générateur de courant: en se déchargeant, il libérerait l'énergie proportionnellement à la quantité maxima accumulée. Dans les cas d'une masse cérébrale où le potentiel générateur est trop élevé, soit par augmentation de la capacité du condensateur ou par diminution du seuil d'excitabilité, il y aurait libération soudaine d'énergie d'autant plus grande que l'accumulation était considérable. Gibbs écrivait en 1937 que le cortex devait être considéré comme une population d'oscillateurs électrochimiques. Plus l'unité est considérable, plus il prendra de temps à se décharger et plus grande sera la charge accumulée. Une batterie capable de produire une forte décharge électrique est nécessairement plus grande qu'une autre de même nature qui produit une décharge plus faible (Gibbs et Gibbs<sup>8</sup>). C'est ce qui semble se produire cliniquement dans l'épilepsie idiopathique où le déséquilibre fonctionnel des systèmes régulateurs centrencéphaliques se fait sentir sur le reste de la masse cérébrale de façon paroxystique et périodique. Dans ces conditions, la réduction de la masse cérébrale aurait pour effet de diminuer la capacité du condensateur, abaissant ainsi le potentiel générateur, élevant aussi le seuil d'excitabilité (seuil convulsivant).

En suggérant cette hypothèse, nous avons détourné notre attention des phénomènes électriques qui se passent au niveau du foyer épileptogène pour observer la dynamique totale de la masse cérébrale, son comportement à l'égard d'un événement inhabituel: la décharge paroxystique. On ne peut nier qu'en certains moments le cerveau est mieux prédisposé à s'enflammer en entier devant l'étincelle initiale d'un foyer soudainement hyperactif.

Il nous semble que plus il y a de masse susceptible de réagir, plus il y a de prédisposition à la réponse épileptique. Dans cette occasion la réduction de la masse diminuerait la quantité de substance réactionnelle. Un foyer localisé peut occasionnellement manifester une hyperactivité électrique, mais n'ayant pas la masse critique prédisposante, il ne peut répondre à la décharge localisée de façon soutenue par une post-décharge auto-entretenu.

Dans une étude expérimentale chez le chien nous avons étudié les modifications du seuil convulsivant métrazolique après réduction de la masse cérébrale par exérèse d'un pôle frontal. Nous avons observé que le seuil convulsivant métrazolique était considérablement abaissé après l'ablation d'une partie de la masse cérébrale. McKenzie, Seguin et Stavarakis<sup>9</sup> ont observé le même phénomène par les procédés d'électro-convulsion chez le chat lobectomisé. Ils avaient noté aussi que ces animaux étaient plus susceptibles à l'action dépressive des barbituriques après résection du lobe frontal. Nous ne pouvons pas établir de relation entre ces résultats expérimentaux et les observations cliniques que nous avons rapportées plus haut.

#### CONCLUSION

L'exérèse unilatérale d'un lobe préfrontal est suggérée dans les cas d'épilepsie *incontrôlable* par toute médication ou toute forme de thérapeutique conservatrice, que l'épilepsie soit d'origine centrencéphalique ou quelle soit d'origine corticale, diffuse, non focalisée.

L'exérèse cérébrale ne porte pas sur une région présupposée lésée où le siège d'un foyer épileptique actif.

L'exérèse du lobe pré-frontal est un procédé *non électif* et n'a pour but que de réduire la masse cérébrale afin de diminuer le potentiel épileptogénique du cerveau entier.

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#### SUMMARY

In recent years the authors have been concerned with the problem of epilepsy uncontrolled by any kind of medical treatment including oxygen therapy, general anesthesia and hypothermia. Cases are presented in which electroencephalographic abnormalities were either of subcortical or centrencephalic origin, or from multifocal cortical regions,

and where it was never possible to demonstrate a precise and constant cortical focus.

These patients underwent ablation of the prefrontal lobe without regard to the side of maximal electroencephalographic abnormalities; the choice of side was based on the cerebral dominance for handedness.

The results of surgery would appear to support the hypothesis that reduction of the cerebral mass diminishes the epileptogenic potentiality of the whole brain.

It would appear that unilateral prefrontal lobectomy might help to control cases of so-called uncontrollable non-focal epilepsy. The seizures could be of centrencephalic or of cortical origin but without any precise and constant localization, as seen in cases of diffuse encephalopathy.

The procedure of prefrontal lobectomy is not directed toward removing an epileptogenic focus. It aims only at reducing the cerebral mass in a possible attempt to decrease the epileptogenic potentiality of the brain mass as a whole.

## A CLINICAL ASSESSMENT OF ANTICOAGULANT CONTROL\*

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### INTRODUCTION

QUICK's one-stage "prothrombin time" determination<sup>1</sup> has gained wide laboratory and clinical acceptance over the past 15 years as a standard of measurement on which clinical treatment with the coumarin or danedione derivatives is based.

Such widespread acceptance has not blinded the eyes of either hematologists or clinicians to the fact that the test is not perfectly satisfactory from either standpoint; certainly to the clinician, spontaneous hemorrhage occurring within the so-called "therapeutic range" of the test has been an uncommon, but frequently disastrous, episode when it occurs.

During the past five years two new tests from Canada<sup>2,3</sup> and Norway<sup>4</sup> respectively have made their clinical appearance. In order to form an opinion as to the possible usefulness of either or both of these tests, in place of the usual "prothrombin time", they have been evaluated clinically using a male hospital population, since both represent a considerable departure in theory and practice from what has been standard laboratory procedure in Canada and abroad.

### METHOD OF STUDY

Sixty elderly male patient volunteers from Victoria Veterans' Hospital were accepted for the study, none of whom gave any clinical or laboratory suggestion of any form of hemorrhagic diathesis.

The "standard" clotting time<sup>2</sup> was performed on all patients by withdrawal of blood from one antecubital vein, followed immediately by an identical withdrawal of blood from the opposite side of the body. All blood samples were drawn from right and left arms, alternately, by one team member, while test measurements were carried out by the second team member, a qualified and

experienced laboratory technician. Only clean venipuncture samples were accepted for the study. On 42 of the 60 patients duplicate Quick one-stage "prothrombin times" and venous "Thrombotests" were also performed. Although the determinations were therefore not strictly simultaneous, it was felt that the procedure used would allow reasonable evaluation of the reproducibility of each test. Each series of tests on all patients was carried out at random times on different days, and all duplicates were blind.

To complete this study of hospital "normals" the capillary Thrombotest was performed on a group of 10 male volunteers, again using blind duplicates.

Finally, both tests have been carried out routinely in the management of patients selected for anticoagulant therapy with phenylindanedione, and the relationship of the two tests has been studied in clinical practice.

### LABORATORY TECHNIQUES

#### 1. Standard Clotting Time

The only modification introduced into this phase of the study was substitution of a "homemade" water bath in place of the type constructed by Mayer himself. It was simply constructed by standing a small insulated metal picnic case in two inches of water inside a larger open picnic case of the same type. The smaller picnic case contained a simple rack to hold capillary tubes, and enough water at 21° C. to give 3-4 cm. coverage of the capillary tubes. By keeping the water in the larger case very slightly warmer, however, to allow for cooling from the entire apparatus, it was quite easy to keep the capillary bath itself at a nearly constant temperature with fluctuations of only 0.1° C. over a 30- to 40-minute period. Otherwise, equipment and technique used in performing the standard clotting time were exactly as described by Mayer. Capillary tubes, adapters and stopcocks were obtained from the same supply sources. Using this technique, three capillary tubes were simultaneously filled with venous blood from one venipuncture by deflecting blood flow from the syringe into the stopcock side-arm, after the first 6.0 c.c. of blood obtained was drawn into the syringe itself. Timing began when the blood entered the capillary tubes. Details of technique described by Mayer

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in breaking the capillary tubes were followed meticulously. As Mayer points out, after an initial period of practice and observation, the determination of the end point is quite sharp.

### 2. Prothrombin Time

For the single-stage prothrombin times, blood samples obtained by venipuncture were collected in 15-c.c. Pyrex graduated centrifuge tubes; 4.5 c.c. of venous blood was added to 0.5 c.c. of sodium oxalate (1.34% sodium oxalate in distilled water). Control plasma and thromboplastin were obtained from a commercial supply house,\* duplicate control prothrombin times of 14-15 seconds being obtained in our laboratory throughout this study. Prothrombin time values, given in this paper in per cent (%), were plotted from saline dilution curves as supplied with the commercial thromboplastin, the appropriate curve being used in each case for the control value obtained.

### 3. Thrombotest

#### (a) VENOUS

In this test the freeze-dried reagent is dissolved in 3.2 mM solution of calcium chloride in distilled water (to maintain optimal calcium concentration when using citrated blood). To 0.25 ml. of this reagent, placed in a "Lusteroid" tube, is added 0.05 ml. of citrated blood, blown from a pipette, and the stopwatch used to measure coagulation time is started. In our tests 0.5 ml. of 3.1% sodium citrate was measured into a special plastic tube, containing a circular mark at 5 ml. Venous blood was then added immediately on withdrawal from the vein by needle and syringe to the tube mark. Reagent and blood were mixed by gentle shaking, and the tube was left in a water-bath (as used in the standard clotting tests) at 37° C. for 30 seconds; at short intervals thereafter, the tube was removed from the water and tilted until coagulation occurred. The end-point is quite sudden and therefore quite easy to record. From the coagulation time in seconds the Thrombotest percentage was read from the venous calibration curve supplied with the reagent.

#### (b) CAPILLARY

For the capillary test, the freeze-dried reagent was dissolved in appropriate amounts of distilled water (depending on ampoule size). Reagent used in both venous and capillary tests was not stored longer than two days at plus 4° to plus 6° C., and was never frozen and thawed out. Thrombotest reagent, 0.25 ml., was then pipetted into a "Lusteroid" tube, and left in a 37° C. water bath for 15 minutes. A sharp-pointed, sterile, disposable scalpel blade was used to make a sharp cut in the finger-pad previously cleansed with ether. Particu-

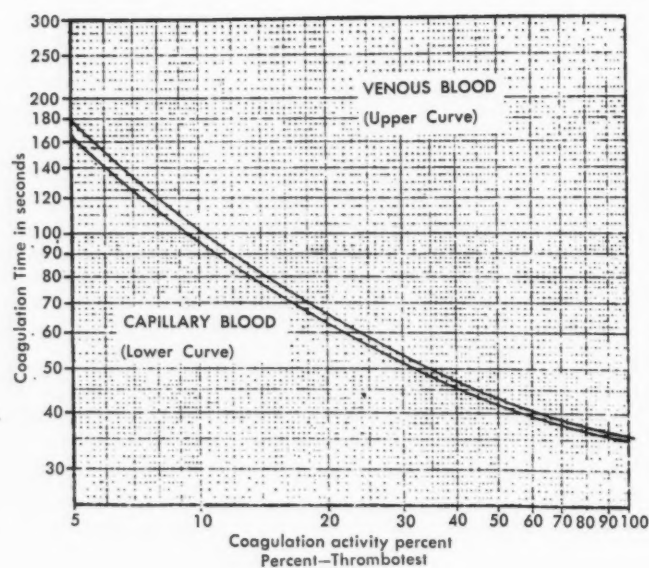


Fig. 1

lar care was taken to obtain free blood flow without milking, and only the first drops of blood were used. Blood, 0.05 ml., was pipetted from the finger and blown into a test-tube, and again the stop watch was started. The rest of the test was carried out as with the venous method, except that the percentage Thrombotest activity was read from the capillary Thrombotest calibration curve, also supplied with the reagent. One of these sets of calibration curves is reproduced in Fig. 1. Special dilutions of blood and reagent, used to obtain greater accuracy in the 50-100% range, were not used in this study.

### RESULTS

#### Standard Clotting Time

Three readings were taken from each arm as previously described, and designated Left 1, 2, 3, and Right 1, 2, 3. Table I shows the mean and standard deviations of the six columns for the 60 subjects.

Analysis of variance revealed no significant difference between the means of the six columns. The means for the left and right arms are 750.7 and 778.0 respectively. It should be noted that in 26 of the 60 subjects the mean of the three readings for the left arm was higher than the mean of the three readings for the right arm. In four subjects the means for the left and right arms were equal. Thus in only half the subjects was the right arm mean higher than the left arm mean. The difference between the left arm mean of 750.7 and the right arm mean of 778.0 for the 60 subjects is due to large differences between the means of the two arms, of more than 200 seconds in eight subjects, with a higher reading for the right arm, against only one such difference for the left arm. A product-moment correlation between the left and the right arm means for the 60 subjects was 0.76.

The range of the mean of three readings for the left arm is from 405.0 to 1320.0 seconds. The total

\*Warner-Chilcott Laboratories Co. Ltd.

TABLE I.—MEANS AND STANDARD DEVIATIONS IN SECONDS FOR THREE READINGS FROM EACH ARM (N = 60).

	Left 1	Left 2	Left 3	Right 1	Right 2	Right 3
Mean.....	719.0	760.3	772.6	756.7	782.0	795.0
S.D.....	164.1	180.8	174.0	179.3	174.7	175.6

mean for all readings is 764.3 seconds, with a standard deviation of 174.8 seconds.

The range shown above for the mean of the left arm readings is from less than six minutes to 22 minutes.

The adequacy of a "sample" mean as an estimate of the "true" mean depends on the number of readings from which it was calculated, and the degree of homogeneity of the readings. The range is one measure of the degree of homogeneity. The range for each set of three readings for both the left and right arms is shown in Table II.

TABLE II.—RANGE IN SECONDS FOR EACH SET OF THREE READINGS FOR THE LEFT AND RIGHT ARMS FOR 60 SUBJECTS

Seconds	Frequency
540 - 599.....	2
300 - 539.....	1
180 - 299.....	5
120 - 179.....	15
60 - 119.....	16
30 - 59.....	43
1 - 29.....	31
0 - .....	7
	120

It may be seen from Table II that in 81 of the 120 subjects the range from the lowest to the highest reading of a set of three is less than one minute. In eight cases the range is more than three minutes and in two cases more than nine minutes.

*Prothrombin Times*

Of 42 duplicate prothrombin times, 33, or approximately 80%, gave duplicate readings of 100%. Results on eight patients varied from 83% to 95%. One patient's prothrombin time was reported as 74%. Four patients showed a variation from one arm to the other, but none of these varied more than 10%. In none of the eight patients mentioned were clotting times abnormally prolonged.

*Venous Thrombotest*

Twenty-eight of 42 patients, or 66%, gave duplicate readings of 100%. Of the remainder, two patients fell in the range of 90% to 100%, two between 80% and 90%, two gave results between 70% and 80%, five between 60% and 70%, and three between 50% and 60%. Duplicate results in these patients differed from one another in only two cases, with a variation of 4% and 13% respectively. Five of these 14 patients with results of less than 100% also gave prothrombin time results of less than 100%, but again, none of the 14 patients demonstrated prolonged clotting times.

*Capillary Thrombotest*

Blind duplicate determinations were carried out on 10 patients. Duplicates varied here in six patients, the greatest variation being in one patient where Thrombotest percentages of 80% and 100% were recorded. All values obtained in the 10 patients fell between 80% and 100%, and except in the one patient mentioned, duplicates varied by not more than 6%.

*Therapeutic Use*

Both the Thrombotest and the prothrombin time have been performed simultaneously on a group of 40 outpatients, providing an opportunity to study the two tests in actual practice.

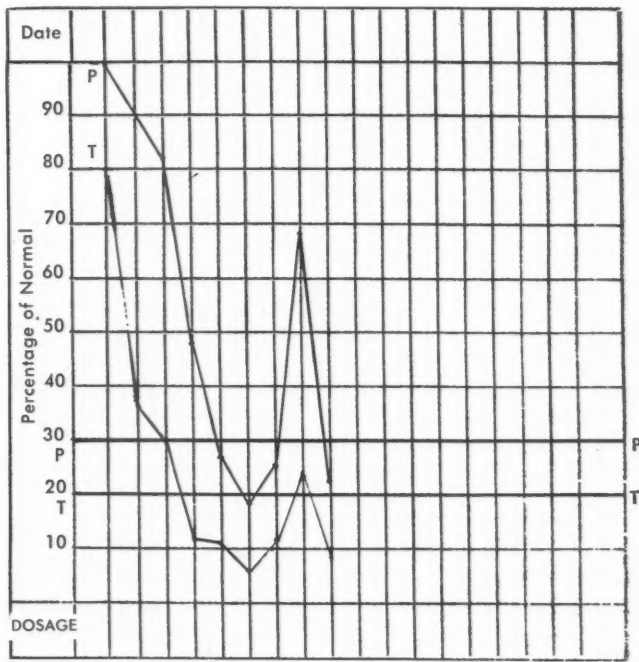


Fig. 2

In Fig. 2 the earlier response of the Thrombotest to phenylindanedione (Danilone) administration is clearly seen; line P-P represents an accepted range of prothrombin activity, and T-T gives a similar value (as advocated by Owren<sup>6</sup>) for the Thrombotest.

Fig. 3 clearly demonstrates a uniform finding in all of our patients to date, and is in agreement with the report of Moore and Beeler,<sup>8</sup> cases that fall within the therapeutic range by the prothrombin time lie in the range of 10% or less by the Thrombotest. This is considerably less than the level suggested by Owren.

A product-moment correlation of the prothrombin times and Thrombotests obtained by 221 read-

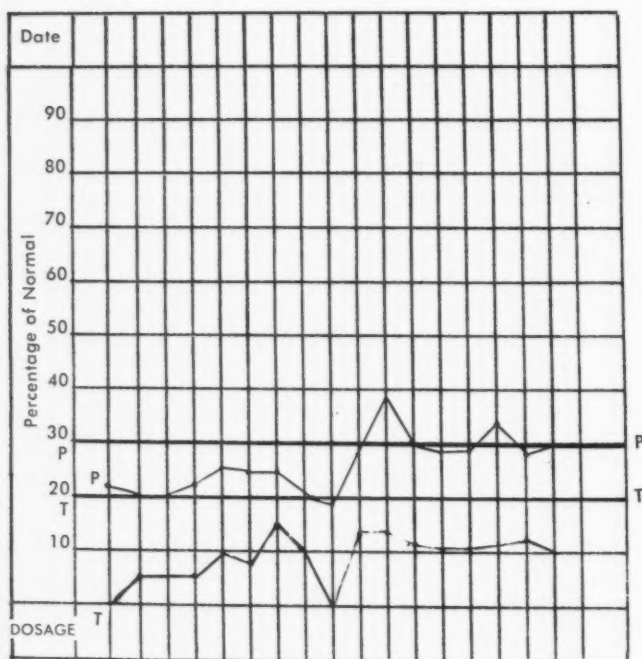


Fig. 3

ings from 34 patients over a period of three months yielded a coefficient of .814.

Fig. 4 illustrates a so-called "difficult" or unpredictable response to phenylindanedione (Danilone). Both the Thrombotest and the prothrombin time tend to fluctuate, but the former within much narrower limits in such patients. Cautious increases in dosage finally brought this particular patient under control.

#### DISCUSSION

The standard clotting time is a reproducible technique, but shows such a wide range of normal values from subject to subject, and (as has been shown) in some cases from tube to tube, as to make interpretation of the control mean in any given patient open to considerable error. Such fluctuation, of course, would have a most important bearing on one's concept of the "level" of anticoagulant activity maintained in one's patients.

The venous Thrombotest is an easy test to perform, and can be learned quickly by inexperienced personnel, as others<sup>5</sup> have shown. In this study, however, it was not an ideal test in the sense that control values of 100% or values reasonably close to this figure were not routinely obtained. As Seaman<sup>5</sup> has pointed out, there may well be a slight fall-off in technical accuracy in the higher ranges of the control curve (see Fig. 1), owing to the inherent characteristics of the curve and the fact that it has been expressly designed to be read within the usual therapeutic range of anticoagulation. This study indicated that control values of 80% to 100% were to be expected, but a definite percentage of values at the 50% to 60% level suggested some factor other than technical error. Such a factor was found in a study of the material itself. Deterioration of the reagent results, when

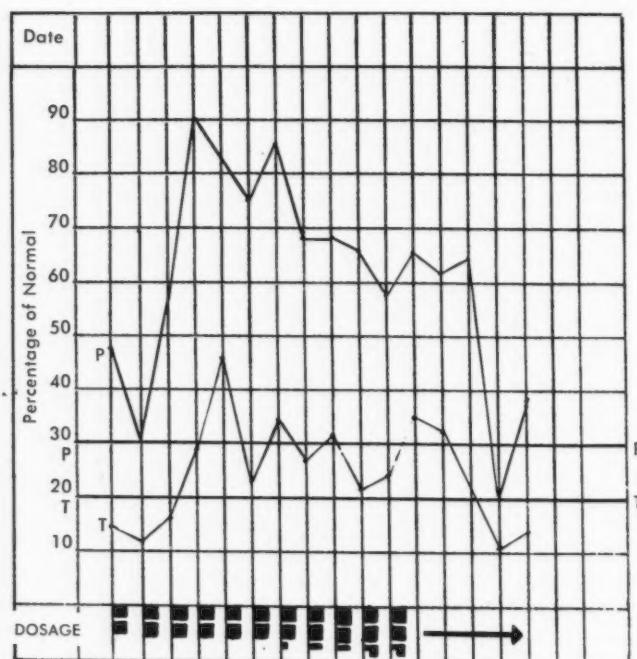


Fig. 4

reconstituted, in a clumpy, flocculent solution instead of a translucent homogeneous one. Such defective solutions invariably show reduced activity, and are caused either by defective vacuum, or prolonged storage at too high temperature.<sup>7</sup> The latter factor, probably occurring in our own laboratory, was felt to be responsible in this study for the reduced activity noted.

Since this experience the reagent has been stored at temperatures never exceeding the 60° to 70° F. range. Control curves (as supplied) have been carefully checked against known normals on all batches of reagent with consistent values of 80% to 100%. The simplicity of the test, and its sharp end point, make duplicate determinations unnecessary, and these have been discontinued.

Experience with the capillary test seems to have demonstrated the following points:

1. Slightly more variation in results may be expected with this test than with the corresponding venous test. However, this variation may be more apparent than real, since it occurred in the range of normal values where the inherent characteristics of the calibration curve reduce accuracy somewhat. Variation between duplicates may well be much less in the more sensitive area of the curve although this was not determined in this study.

2. The original technique of using 0.1 ml. of capillary blood detracted seriously from its usefulness as a relatively simple clinical procedure, since patients tended to object strenuously to the trauma necessary to obtain this amount of freely flowing blood from a stab wound. The newer "half-dose" technique, as developed by Owren and now presented in the literature circulated with the reagent, has removed this problem. With the capillary method, results are available from the laboratory within five minutes of the patient's arrival.

#### RATIONALE OF THE THROMBOTEST

Two pathways for blood coagulation are postulated:<sup>4</sup> one utilizes "intrinsic" thromboplastin with relatively slow clot formation; the other utilizes tissue thromboplastin with coagulation occurring much more rapidly.<sup>4</sup>

Most authorities seem to agree that indirect anticoagulants act by inhibiting the rate of synthesis in the liver of coagulation proteins, including Factor II (prothrombin), proconvertin (Factor VII), plasma thromboplastin component (Factor IX or Christmas Factor) and Stuart Factor (Factor X). "During treatment with dicoumarol-like drugs, both the intrinsic and the extrinsic coagulation systems are depressed, the former through reduction of Factor IX, the latter through reduction of Factor VII. Reduction of the Stuart-Prower Factor and prothrombin influences both systems." The activity of these two coagulation systems in the Thrombotest has therefore been adjusted by accelerating the intrinsic process with an active cephalin preparation, and retarding the extrinsic system by the introduction of a thromboplastin of low activity.

Needless to say, all authorities do not necessarily agree with the composition of the reagent, and what process or processes are actually measured by the test.<sup>9, 10</sup>

#### CONCLUSIONS

This study of two newer methods of controlling anticoagulant therapy confirms both as reproducible clinical techniques.

Both tests demonstrate possible disadvantages which must be considered in the choice of a method for clinical control of anticoagulant treatment.

In patients receiving satisfactory anticoagulant therapy from the standpoint of the prothrombin time, unexpectedly low Thrombotest values were obtained. This raises a question as to the degree of interference with prothrombin activity necessary to obtain clinically satisfactory results in the treatment of arteriosclerotic disease. Such information will undoubtedly come from adequate clinical trials using alternate methods of control.

#### SUMMARY

Two tests, the standard clotting test and the Thrombotest, have been compared in a group of hospitalized patients.

Reproducibility and possible defects of both tests are discussed.

Clinical experience with the Thrombotest, in a group of 40 outpatients maintained on anticoagulants, is reported.

The authors wish to thank the nursing, laboratory and outpatient staff of the Victoria Veterans' Hospital for their interest and co-operation in this project. Mr. Spencer, clinical photographer at St. Joseph's Hospital, was responsible for the tables and figures.

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#### PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

##### TRANSIENT ATTACKS OF APHASIA AND PARALYSES IN STATES OF HIGH BLOOD PRESSURE AND ARTERIO- SCLEROSIS

The mode of origin of these cerebral crises in arterio-sclerosis has been much discussed of late years. When Peabody brought forward the view that in these cases a transient arterial spasm occurred, I was doubtful how far this was possible in sclerotic vessels; but I have since come round to his view and I do not think any other explanation is more plausible than that these attacks represent vascular crises.

We have plenty of evidence that arteries may pass into a state of spasm with obliteration of the lumen and loss of function in the parts supplied. In the peripheral arteries in Raynaud's disease we can sometimes feel the spastic, cord-like vessel; in the retina we can sometimes see the arteries contracted. Both in Raynaud's disease and in the remarkable thrombo-angitis described by Buerger the obliteration may persist until necrosis occurs, but in many instances it is only transient and the circulation is restored. A case of Raynaud's disease, with recurring attacks of aphasia, hemiplegia, and loss of consciousness, some occurring coincidentally with the local asphyxia and necrosis, convinced me that intermittent closing of the cerebral vessels could occur, and the transient nature of the

attacks with the complete recovery seems to offer no other explanation so satisfactory. And we know now that there are neither anatomical nor physiological objections to this view as applied to the cerebral arteries.

Transient paralyzes in uraemia may be due to oedema, as suggested by Traube, but this condition is rarely transient and is more often a terminal event. It is possible that there are cerebro-spinal manifestations in angio-neurotic oedema, as in the extraordinary case which I reported of a physician, aged twenty-nine, who had right hemiplegia and aphasia at the age of nine, and, within a year, five or six attacks of transient hemiplegia, subsequently migraine, and well-marked attacks of angio-neurotic symptoms. Howland has recorded a case of this disease with spinal symptoms. The association of migraine with cerebral symptoms is well known, and Mitchell Clarke has reported a familial form with which hemiplegia occurred in three generations.

The diagnosis, usually easy, is based on the existing conditions of high tension or sclerosis or both, the slight and transient character of the attacks, and the recurrences. Slight paralyzes due to haemorrhage of softening rarely pass away so quickly, and it may be weeks before a patient speaks clearly or uses the hand freely. Numbness, tingling, and slight weakness of one side with headache may be precursors of a "stroke", in which case the symptoms are not transient but progressive.—Sir William Osler, *Canad. M. A. J.*, 1: 919, 1911.

## VIEWPOINTS

### CONTROLLING THE CHAOS

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IN NEW YORK CITY the Physician's Council, an independent group made up of 18 eminent physicians, was organized in 1956 "to seek means of maintaining high standards for the material on health that is disseminated through the media of mass communication". A brief, recently submitted to this Council, was endorsed by them as accurate, equitable and constructive, and was subsequently published.<sup>1</sup> In this brief, Dr. Charles D. May analyzed the present-day relationship between the medical profession and the pharmaceutical industry. The present paper will discuss the reasons for the existing situation, and outline in detail a proposal to alleviate it.

Dr. May described the principal deleterious elements in the medical-pharmaceutical relationship as follows:

1. The medical profession is being deluged with promotional material from pharmaceutical houses which presents a picture blurred by multiple brand names, conflicting claims and misleading statements. Merchandising is emphasized at the expense of service to the profession, and an artificially manufactured complexity has unnecessarily complicated the treatment of disease.

2. Increasing sums are being spent on drugs; there has been a steady rise in the use of drugs; and over-the-counter sales are booming. In the U.S.A., the Food and Drug Administration and the Federal Trade Commission are neither empowered nor equipped to deal effectively with this situation.

3. Acquiring information through medical journals is difficult, in part because of the steadily increasing number of journals; and because many of them are edited and their contents written by journalistic amateurs who pay too little attention to selectivity and format. However, acquiring information from what Dr. May aptly calls the paramedical literature, published by pharmaceutical houses, is easy. They provide a well-presented subtle indoctrination, the persuasive force of which is supplemented by various forms of subsidies to individual practitioners, medical journals and professional organizations.

All of this is true, and it is interesting to trace how it has come about. Until approximately 25 years ago, the study of *materia medica* consisted largely in the memorizing of long lists of galenicals, their doses and incompatibilities. Departments of pharmacology taught the effects of these drugs, the indications for their use, and means of exhibiting them. Great emphasis was laid on prescription writing, and a great part of therapy was by means of mixtures compounded by the local pharmacist

for the individual patient. Those proprietary mixtures which were in use were tried-and-true formulas whose attraction lay in the improved elegance of large-scale manufacture. These mixtures carried special names, easily remembered because they were directly derived from the generic names of the ingredients or were related to the symptoms to be relieved. A distinction was made between "ethical" houses, manufacturing compounds exclusively for the use of physicians, and "non-ethical" firms who made patent medicines, but frequently a prescription compound of time-honoured reputation was translated into a popular patent medicine.

Then came the era of specific therapy. The synthetic chemist and the physiologist, spurred on by the exigencies of war, discovered and developed one miracle drug after another—drugs which would attack a specific deleterious influence in the body and control or eradicate it. Previously incurable diseases paled into minor misfortunes, easily overcome. Emphasis in medical writing was transferred from diagnosis to treatment; no article was complete without at least some effort to show an improved method of treating the condition described, preferably with a previously unknown drug. These new therapeutic agents were given approved "generic" names arrived at by various means because the nomenclature of the synthetic chemist does not easily lend itself to use on labels and advertisements. From this latter point of view, even the approved generic names were not satisfactory to the pharmaceutical manufacturer, and so brand names were selected and registered for the exclusive use of each company marketing a given drug. The rationale for this practice is exemplified in a list of approved (generic) and proprietary names published recently,<sup>2</sup> in which of 22 names listed, 21 of the approved generic names were much longer and less easily pronounced or written than the corresponding proprietary brand name. Naturally enough, remarkable drugs were given remarkable brand names, and since the same compounds were being marketed by several firms, the brand names of drugs began to assume the same importance from the point of view of merchandising as the brand names of soaps and motor cars.

Of the physicians practising today, approximately one-half graduated from medical school during the latter part of the earlier era. For these men, all knowledge of modern specific therapy has been derived from medical journals, professional meetings and information supplied by pharmaceutical houses. Articles in medical journals are written, and medical societies are addressed, by cautious practising physicians who tend to be conservative in their appraisals of new remedies, and to publish such appraisals only after a considerable number

of patients have been treated. The pharmaceutical house, however, by combining the results of numerous clinical trials scattered over the world can present what appears to be substantial evidence in a relatively short time. Thus sufficient investigative work to satisfy the present regulatory bodies can be accumulated quickly, and a drug can be launched with widespread journal advertising and attractive brochures outlining the available clinical experience, long before any individual feels competent to commend or condemn the drug on the basis of his own work. The impact of such promotional campaigns on men educated in the earlier tradition was easily foreseen. The younger graduate, who might be expected to be more skeptical, usually obtains a post far down on the professional ladder, and in a short time his thinking is greatly influenced by the methods of his seniors.

Concomitant with this development was another which was perhaps even more significant. The discovery of new drugs which produce seemingly miraculous cures is "news", not only to medical readers, but to laymen the world over. The popular press seized this new source of interesting material with alacrity, and a whole new specialty of pseudo-scientific writing came into being. A facile writer is able to take evidence which any physician would regard as merely being suggestive and construct on this slender material the story of a modern scientific miracle. This has been done over and over, until today physicians say somewhat wryly that they must read the popular magazines in order to keep abreast of the latest developments in medicine. Patients demand from their doctors therapies not yet completely reported in medical journals. This factor alone has imposed tremendous pressure on the medical profession to employ "new" remedies as soon as possible; as one writer has put it, we must make haste to employ new drugs before something better is discovered.

Prosperity is still another factor. People who enjoy a high standard of living do not hesitate to demand the latest "fashionable" therapy, nor do they object to paying a high price for it. In the past few years, there has been a great upsurge of interest in "do-it-yourself"; this has been encouraged by reams of writing on such topics, and the introduction at the home level of materials and processes formerly known only to industry. Medicine has been no exception: articles written for lay readers have made do-it-yourself physicians out of countless laymen, who have proceeded to treat themselves and their friends with every medication whose sale is not restricted. As Dr. May points out, over-the-counter sales are increasing steadily, but this is the fault of the patient and his journalistic advisers more than of the pharmaceutical houses. Our economy is built on the principle that if there is a demand for any commodity whose sale is not restricted by law, the demand will be met.

Combative measures against this rising tide of ill-advised, ill-timed, useless or frankly harmful medication, whether professional or self-administered, have been uncoordinated, weak and ineffective. Doctors practise as individuals, think as individuals, and are notoriously loath to adopt a uniform or regimented view on any subject. Hospitals have shown little or no willingness to adopt uniform regulations, and universities defend hotly their right to teach what they will. Pharmaceutical manufacturers, on the other hand, are well-organized businesses doing a straightforward job of merchandising in which they employ all available means. It is doubtful that there is a greater proportion of villains in the pharmaceutical industry than in any other; the majority of businessmen are trying to sell the best possible product to the greatest number of people, and so are the drug manufacturers. They are inspired by high idealism to exactly the same extent as are the rest of us, subject to the same frailties, motivated by profit and bedevilled by stockholders.

What, then, is to be done about it? We have arrived, for the reasons given, at a situation in which the laws of supply and demand, the checks and balances of food, drug and trade regulation, the accepted rules of professional conduct and the present means of communicating medical information are inadequate to protect us from deleterious and quite possibly catastrophic results if adequate remedies are not found. As one British writer recently stated,<sup>3</sup> "The interrelations between profession and industry are highly complex, and close analysis of these is called for if treatment is to be based on information and not persuasion, and if the practitioner is to maintain his freedom to prescribe what is best for his patient. Without this freedom the practice of medicine will deteriorate and the patient will suffer. To preserve this essential freedom, profession and industry must search their consciences and together establish some code which will enable them both to utilize to the full the tremendous benefits brought about by the current revolution in medicinal therapeutics."

Two things only are needed. The first is education at all levels. In so far as the medical profession is concerned, it is essential that all our universities include in their curricula of pharmacology and therapeutics clearcut presentations of the pitfalls of drug therapy today. The Associations of Medical Colleges in as many countries as possible should draw up and adopt a uniform course outline, which describes the methods by which drugs are developed, their assessment, clinical trials, the elements of statistical evaluation, the laws governing marketing, the ethics of publication to lay audiences, and the place of the profession as guardians of a valuable and potentially dangerous therapy. This course should have equal importance to, say, Medical Jurisprudence and Toxicology.

Medical journals must assume a share of responsibility, too. Not only should editors ensure that this

important topic is kept before the profession, but they must also assume responsibility for improving the readability and format of their publications. A good editor can make or break a paper whose content may be extremely important but is obscured by poor presentation. In no other field is there so much reluctance to improve the style or clarity of contributors; many of us have something worthwhile to say, and there are few of us who cannot with help be made to say it better.

The public must be educated, as well. The existing widespread interest in scientific and particularly medical subjects can be turned to good advantage if an effort is made to show laymen the problems with which we are faced, and the steps being taken to safeguard our patients. One step we must avoid is the limitation of over-the-counter sale of those drugs which can safely be marketed in this way. True, "safely" is the operative word, and one might well argue that aspirin and iron are potentially toxic drugs, but a reasonable approach must be maintained. Where the hazard is no greater than with many cosmetics, the average citizen has the right to purchase freely his dietary aids, tonics, throat pastilles and cough syrups. To restrict these on the ground that the increase in self-medication is professional suicide is not only nonsensical, it will most certainly bring loud protests that the medical profession is fostering an illegal combine for personal gain. Cosmetics were mentioned above; we have greatly improved our means of controlling these in the past 20 or 30 years; we can do the same with proprietary drugs.

Finally, we must educate the pharmaceutical industry. We owe them a great deal for their part in the development of new drugs, and we can discharge much of this debt by paying them the compliment of subjecting their products to careful scrutiny before prescribing them. The advertising material which chokes the doctor's mailbox is much like a legal contract; if the drug manufacturers find that we are taking time to read the fine print, they will respect us more, and dishonest presentations will gradually disappear. Detail men are unaccustomed to being asked how well a clinical trial was controlled, and some of the inquiries directed to them show such a shocking unwillingness to search out basic information from professional sources that it is no wonder they have a low regard for the physician's discrimination. Once it is made clear that the medical profession is determined to regulate the use of drugs, to use the indicated medication correctly and to stop prescribing either a wrong or useless drug or a right drug in a wrong or useless manner, the pharmaceutical manufacturers will compete with each other to please us. The information they give us will be as accurate as we demand that it be—no more, and no less.

Since drugs are made and prescribed by mortals, however, education alone is not enough. We must have legislation, and if it is adequate and enacted

soon enough, it can be legislation framed and administered by professional physicians and pharmacists. If it is not, it will be imposed by laymen for the protection of the community; of that, as the late W. S. Gilbert said, there can be no shadow of doubt, no shadow of doubt whatever.

The surprising thing is that we have gone on thus long without legislation that is neither impotent nor edentulous. In Canada,<sup>4</sup> at present, a measure of control is exercised by the Department of National Health and Welfare through its Food and Drug Directorate, under authority from four separate Acts of Parliament. This control is concerned principally with advertising and labelling of foods, drugs, cosmetics and therapeutic devices, and is designed primarily for the protection of the public. Requirements are laid down which must be fulfilled before a new drug may be marketed; these again are mostly concerned with safety rather than with therapeutic usefulness. There is no power conferred for the Department to give approval of a label or advertisement; the only alternatives appear to be active disapproval or silence. The limitations of existing controls are illustrated in a letter received by the writer recently. A complaint had been sent to the Minister of National Health and Welfare about the distribution of samples of well-known tranquilizers in unsealed second-class envelopes, the samples being plainly visible through a cellophane "window" in the envelope. These samples are, of course, of drugs on the "prescription only" list. In his reply, the Minister said, in part: "I share your concern for the indiscriminate distribution of samples of this and similar drugs to physicians in unsealed envelopes. It is doubtful whether we have the authority under the Food and Drugs Act to prohibit the distribution of samples. . . ."

In the United States,<sup>5</sup> apparently, things are not much better. There, the Food and Drug Administration directs its activities mainly toward promoting purity, standard potency and truthful and informative labelling of foods, drugs, tea, poisons and milk. New regulations made effective February 1961 require that literature promoting the sale of prescription drugs must include information pertaining to "relevant hazards and conditions in which the drug should not be used". Recommendations are now before Congress that the F.D.A. be given authority to require proof of effectiveness as well as safety of all new drugs, to require the submission of reports of clinical experience, to strengthen existing inspection authority, to ensure adequate control of manufacturing and packaging; other recommendations advise the co-ordinating of supervision of labelling, promoting and advertising which is now divided among several agencies, the maintenance of research programs and the establishment of an advisory organization of scientific and technical experts.

The fact that we have carried on with such a limited and inadequate system of controls is proof

of the respect which the public accords the medical profession; what we must do at once is ensure that the respect is deserved. We need a Commission of Pharmaceutical Regulation, and in North America at least, this should be on an international level. It should be composed of representatives of the medical profession, the pharmaceutical industry, the universities, and, in an ex-officio capacity, of government. Its members should serve full time, having been nominated by the bodies they represent, and be as free of political influence as the judiciary. An adequate secretarial staff to take care of a very large volume of work will be required; on the other hand, much of the work of existing agencies would be turned over to the Commission.

The cost of this commission should be met by (a) government subsidy, because the people as a whole are being protected; (b) the pharmaceutical industry, perhaps from a percentage of advertising appropriations because uniform standards of excellence will be maintained; and (c) the medical profession through the sale of informative publications.

The functions of the Commission should be these:

1. Absolute control over drug nomenclature. Insistence that single drugs, as opposed to combinations of drugs, should be known by approved generic name only, which will be followed by the name of the manufacturer in promotional material and on prescriptions, etc. Combinations of two or more drugs will be allotted brand names chosen by the manufacturer, subject to veto on the grounds of confusion, or that the compound has been created for commercial rather than therapeutic reasons.

2. Power to rule on the adequacy of experimental work, clinical trials, etc. All promotional literature, advertisements or other related publications should, when the Commission is satisfied that such background work is adequate, and has verified the inferences and statistical conclusions, carry a seal of approval. This seal must be subject to withdrawal if claims are in any way misleading, or if in the light of subsequent work further investigation is indicated.

3. No control whatever over prices, discounts or any part of the financial side of drug manufacture; prices are self-regulating except when the customer does not know exactly what he is buying. The work of the Commission in regulating claims made for drugs will ensure that the physician sees them in true perspective; prices will become realistic very quickly. Competition will again become a real factor when it is made obvious which drugs are competing with each other.

4. No control whatever over existing or future laws regarding patents and copyrights. The manufacturer is entitled to the same protection accorded to originators in other fields.

5. The right to have a manufacturer appear before a court of law if he refuses to comply with Commission rules and regulations. If arbitrary powers are assigned to such a Commission, it would be impossible to avoid political influence, lobbying and sundry other evils. The Commission must have its own legal staff, in each jurisdiction or country in which it operates, to look after the prosecution of non-cooperating manufacturers or distributors.

This, then, is the blueprint we must follow if we are to prevent the development of a much worse state of affairs than now exists. Five years ago it was estimated that about 140,000 medications were in current use in the U.S.A., of which some 90% did not exist 25 years ago.<sup>6</sup> Some countries have followed a policy of laissez-faire in so far as pharmaceutical manufacture is concerned, and are appalled by the resulting chaos. Medicine, pharmacy and synthetic chemistry are all moving very quickly, and it is incumbent on us to safeguard the future. We have recognized our errors; Dr. May is but one of many writing and speaking about this pressing problem. If we wholeheartedly accept our responsibility, the job can be done with a minimum of discord and recrimination. It is really not important who among us is primarily responsible for our plight; the important thing is to remedy it as quickly and efficiently as possible. If we present government with sincere, vigorous and practical suggestions, they will be delighted to turn this political hot potato over to a governing body such as has been described. The thoughtful and farsighted men in the pharmaceutical industry will co-operate eagerly, because they cannot help but realize that some sort of control is long overdue, and that control of the type outlined will in the long run do the industry, the profession and the public nothing but good.

All of us agree that a problem exists. We may, like the blind men palpating the elephant, assess it differently depending on our point of view, but we must admit its existence, and the pressing need for a solution. We protest against encroachments on our professional freedom, but unless we take the initiative in this situation, further loss of independence is inevitable. We must take every possible opportunity to press for the twin remedies of organized education and effective legislation. If we can succeed in having a Commission appointed as outlined above, the destructive potential of the current "drug explosion" can be transformed into useful energy, and generations to come will look back to this turning point in our medical history.

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**SPECIAL ARTICLE****A SUSTAINING SERVICE FOR  
DISCHARGED MENTAL  
HOSPITAL PATIENTS**

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THIS PAPER describes a pilot project which established a co-operative project between a community outpatient psychiatric clinic and a provincial mental hospital, so that better aftercare could be given to the hospitalized patient through closer contact between the staff members of the two organizations. After discharge from a mental hospital, 80 patients were treated by two psychiatric teams consisting of a psychiatrist, a social worker and a nurse. An additional 20 patients who were attending an adult psychiatric outpatient clinic but had never been in a mental hospital were also treated by these teams.

The Adult Clinic of the Mental Health Centre was established, as a branch of the Provincial Mental Health Services, in January 1957 to provide psychiatric outpatient and day-hospital care. Patients come to this clinic, on medical referral, either from the mental hospitals or from their own communities. Six months after the inauguration of the Adult Clinic, it was apparent that about one-half of the patients attending the clinic had been discharged within the previous year from the Provincial Mental Hospital and its acute treatment division, the Crease Clinic. All these patients enrolled in the adult clinic had sufficient insight and motivation to attend voluntarily. Outpatient service was not offered to those who required a great deal of supervision and who remained in the community only through sufferance of family; that is, their families provided a mental hospital service within their own homes. From the first, the Adult Clinic placed emphasis on treatment by therapeutic interview and on the provision of a day-hospital type of program. Tranquillizing medication was used in about half the cases, and only minimal use was made of electroshock and sub-coma insulin.

Formally beginning on August 13, 1957, a special type of service was developed within the Adult Clinic to provide continuing psychiatric care for those patients in the community who did not have the ego-strength to develop further insight or the potential of improved adaptation through psychotherapeutic or intensive casework services. This "sustaining service" clinic met one evening during the month and was staffed by one psychiatrist, one social worker, and one nurse.<sup>7</sup> It was planned that each patient would be seen once a month by either

a psychiatrist or a social worker for a brief re-assessment, reassurance and regulation of medication. A social club was organized, concurrently, through the initiative of other patients attending the clinic and through the participation of the clinic staff and volunteer members of the Canadian Mental Health Association. After a short period, the social club and the Sustaining Clinic were scheduled on the same evening to give the Sustaining Clinic patients more opportunity for social participation, in the hope that they could be maintained on a social rather than medicinal basis. Although any patient enrolled in the Adult Clinic might attend the social club, those reporting for regular interview therapy did not attend the Sustaining Clinic on the same evening. Accordingly, a group of approximately 25 patients were seen in the Sustaining Clinic on one evening each month between 6.00 and 9.00 p.m.

On November 18, 1958, the second Sustaining Clinic was established by the participation of a psychiatrist and social worker from the Provincial Mental Hospital. Nursing service, including prescription service, was provided at the Adult Clinic. The program then consisted of two sustaining clinics each available once a month on alternate Tuesday evenings with a maximum of 25 patients in each clinic. On the intervening Tuesdays, a psychiatrist and a social worker provided longer interviews for ten discharged hospital patients. By the allocation of one evening per week by each clinical team, 35 patients were managed at any one time for a total of 70 patients.

This activity was supported by the regular outpatient clinic services such as aptitude testing for job placement, assistance in finding work or accommodation, emotional first-aid service, and day-hospital service for psychotic relapse if these became necessary. (The Day Hospital, a facility which is open from 8.30 a.m. to 4.00 p.m., has available occupational and recreational activities and personal nursing service (one nurse to five patients). Physical treatment is given in the morning when necessary. The average stay is 37 days.)

The entire plan was designed to accelerate the development of the community aspects of the Provincial psychiatric service in an effort to fill an obvious deficiency in follow-up service to hospitalized patients.<sup>1</sup> The following principles were kept in mind: (1) the maintenance of the "socially remitted" case (sufficient symptomatic improvement to warrant medically approved discharge from mental hospital) in the community at his best level of function; (2) the continuation of restorative psychotherapy initiated in hospital after the patient no longer requires hospitalization; (3) the provision of more adequate training and experience for the professional staff with a view to main-

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TABLE I.—COMPARISON OF GROUPS STUDIED

	Average age (years)	Number of interviews	Marital status	Diagnosis	Symptoms	Social adaptation
Group A (10): Sustaining service (hospitalized)	41	17-38	9 single or divorced	Psychosis (schizophrenic) —10	Severe and chronic, e.g. flat affect, ideas of persecution	Dislocation and/or conflict
Group B (10): Sustaining service (not hospitalized)	42	11-28	5 single	Psychosis —3	Anxiety, inadequacy, depression	Limited
Group C (10): Interview service (not hospitalized)	34	15-38	7 married	Psychosis —1	Anxiety, dependency, somatic symptoms	Limited, often with conflict
Group D (10): Interview service (hospitalized)	38	15-83	5 single	Psychosis —2	Anxiety, lack of confidence, behaviour disturbance	Conflict

Total—40.

taining standards and assisting staff recruitment; (4) the incorporation of this service with any future proposed community mental health plan; (5) the early implementation of this service with present staff establishments.

The cost of the service was borne by the Provincial government. Many patients presented problems that the family doctor<sup>6</sup> was unable or unwilling to deal with himself and/or the patients were unable to afford medications. In some instances, patients attended the clinic but were asked to have their prescriptions filled privately at their own expense.

## EVALUATION

### I. Comparison of Twenty Sustaining Service Patients with Twenty Interview Therapy Patients

We wanted to evaluate the results achieved by the sustaining service and compare these with the results achieved at the Adult Clinic by regular interviews. Interview service is defined, for this purpose, as treatment by formal interviews, approximately one hour in length and at least weekly in frequency. Sustaining service is defined here as treatment by brief contact, usually monthly, with provision for more intensive short-term assistance when the patient becomes decompensated, i.e. the development of symptoms of anxiety or overt symptoms of mental illness.

Four groups, each of ten patients, treated at the Mental Health Centre Adult Clinic over a 2½-year period are compared (Table I).

*Group A. Sustaining service for previously hospitalized patients.* This group consisted of patients who commenced treatment within one year of discharge from the Crease Clinic or the Provincial Mental Hospital. These patients were seen for at least 12 months, the principal treatment being monthly visits to a psychiatrist or a social worker at an evening clinic. Attendance was encouraged at the patients' social club meeting the same evening on the premises. These patients received no formal psychotherapy, casework, or any type of

day-hospital program aimed at improving social adaptation. Medications and specific services, such as phone calls in times of panic, extra visits, job assistance, brief contact with family members or short day-hospital admission, were provided as required.

*Group B. Sustaining service for patients not hospitalized within one year.* The treatment service was the same as that provided for Group A.

*Group C. Interview service (psychotherapy or casework) for patients who were not hospitalized.* This group consisted of patients who had not been hospitalized in the Crease Clinic or Provincial Mental Hospital within one year of the time they came to this service, and whose principal treatment was 15 or more psychotherapeutic interviews. If a family member was also interviewed, such interviews were less than 15 hours. Group therapy attendance, if initiated, was not continued for more than one month. There was no participation in day-hospital programs for longer than one month. Medications and sporadic specific services were provided as required.

*Group D. Interview service (psychotherapy or casework) for previously hospitalized patients.* This group differs from Group C in that all these patients commenced treatment within one year of discharge from the Crease Clinic or Provincial Mental Hospital.

Service to Groups A and B was provided jointly by the Adult Clinic and mental hospital team.

Service to Groups C and D was provided by Adult Clinic staff during daytime.

## SELECTION FACTORS

All patients came to the Adult Clinic on medical referral<sup>6</sup> and were admitted for treatment on the basis of a clinical judgment that their psychiatric disorder could be modified by treatment. It is assumed that the method of treatment offered was appropriate to each case. Patients were excluded from this study if treatment was incomplete or overlapping within the terms defined. Nineteen of the twenty patients in Groups A and B and seven

of the twenty patients in C and D received tranquillizing drugs. Only one patient (Group B) received occasional E.C.T. Much more service was provided to relatives of patients in Groups C and D than for A and B. The subdivision into groups is retrospective but was carried out by means of record office punch cards and did not involve screening by any criteria other than those specified.

#### RATING SCALES

We used the diagnostic and statistical manual of the American Psychiatric Association in an effort to describe the results of treatment in meaningful terms instead of the traditional terms "recovered, improved and unimproved". We have used three scales, the first one being derived directly from the American Psychiatric Association manual:

1. Impairment—a performance scale.
2. Emotional distress—a scale of subjective discomfort.
3. Social tension—a scale of relationships.

The five points defined on each scale can be summarized as shown in Table II.

#### Examples of the Response of Patients to the Program

Group A.—A 48-year-old female patient with schizophrenia discharged after four years in mental hospital, was unemployed and required much family supervision. She was prone to lose control of her emotions and behaviour, was in frequent open conflict with family and had no outside interests. Subsequently, after 27 contacts between the patient and clinic personnel she remains on Social Assistance but has acquired some capacity for self-care. She lacks emotional warmth but no longer has objectionable outbursts, and enjoys social club and family activities. Her rating before entering the program was 555 and after was 443.

Group A.—A 47-year-old female patient with schizophrenia, discharged after 17 years in mental hospital, was employed marginally as a domestic; she was emotionally flat, lacked friends, and her relationship with her father was marked by dependency and hostility. Subsequently, after 23 contacts, and another three-week stay in the mental hospital, she obtained a better-paid domestic posi-

TABLE II.

	<i>Impairment</i> (performance)	<i>Emotional distress</i> (subjective discomfort)	<i>Social tension</i> (relationships)
None.....	1. Effective	Emotions enjoyed	Single and social satisfactions
Minimal.....	2. Pre-illness function	Symptoms appear only under pressure	Structured relationships
Mild.....	3. Impaired under pressure	Symptoms present—mild	Constricted relationships
Moderate.....	4. Maintains self at lower level	Symptoms present—marked	Unsatisfying relationships
Severe.....	5. Supervised	Loss of control	Marked social conflict

For the results of the application of this form of assessment see Tables III and IV and examples.

#### RESULTS

TABLE III.—RATINGS AT ADMISSION TO ADULT CLINIC

	<i>Impairment</i> moderate or severe	<i>Distress</i> moderate or severe	<i>Social</i> <i>tension</i> moderate or severe
Group A*.....	10	8	10
Group B.....	3	8	5
Group C.....	3	8	5
Group D*.....	6	8	5

\*On the rating scales the most severely disturbed patients at the outset were those previously hospitalized.

TABLE IV.—RATINGS AT CLOSE OF THIS STUDY  
(Number of patients in each category who showed improvement).

	<i>Impairment</i>	<i>Emotional</i> <i>distress</i>	<i>Social</i> <i>tension</i>
Group A.....	4	3	7
Group B.....	6	8	7
Group C.....	3	9	4
Group D.....	4	6	2
Total.....	17	26	20

Over three-quarters of the patients recorded as showing improvement rose only one point on the scale (see rating scales).

tion. Despite periodic delusions involving fear of other people, she attends the social club regularly and has established a circle of friends amongst ex-patients. Her rating before attendance at the clinic was 445 and after, 453.

Group B.—A 44-year-old male patient, diagnosed as an "inadequate personality", was employed as a messenger. He suffered from frequent episodes of panic, his social outlets were few and unsatisfactory. He is maintained without medication, his panic has gone; his attitude remains cocky but he now enjoys family activities. His ratings before were 344; now they are 333.

Group B.—A 39-year-old male patient with schizophrenia was unemployed, was hallucinated and avoided people except for his room-mate; subsequently, after 20 contacts in this clinic, he is employed as an unskilled labourer in a lumber yard. His hallucinations have lessened but his shyness is considerable; he belongs to a religious group and has a few friends. His ratings before attending the clinic were 544; now they are 233.

#### DISCUSSION

The original aim in establishing sustaining clinics for mobilized, ex-hospitalized patients with a long

history of illness, was to avoid periodic re-admission by offering regular contacts.<sup>5</sup> The work was approached enthusiastically<sup>7</sup> and after 2½ years beginning August 13, 1957, the goal was realized in all but one patient in Group A; this person had to be re-admitted to hospital. After 3½ years, there have been three brief hospital re-admissions in Group A. The improvement in the level of functioning of a number of severely disturbed patients while on sustained service has been outlined (Tables III and IV) and illustrated by examples given with these tables. The improvement in certain patients given interview therapy has been presented in the same tables. Some of the differences of the groups under consideration have been noted. A number of patients who started on the sustaining service have been transferred to the interview service, and did not meet the criteria for inclusion in this study. The original decision regarding selection for therapy considered not only the symptoms and dynamic pattern, but also the patient's motivation and preference for one kind of service over another. No effort has been made to distinguish between the contribution of the psychiatrist and the social worker or to allow for different degrees of experience or different types of approach of individual therapists.

Among the 40 patients in the study, 31 were born in Canada; the remaining nine foreign-born subjects were distributed evenly among the four groups. There was also an even distribution in religious affiliation: Anglican, eight; United Church, eight; Presbyterian, three; other Protestant, eight; Roman Catholic, six; Other, seven.

The majority, 13, of the 20 patients in Groups A and B of the sustaining service were living in primary family relationships. Seven patients in Group A were living with a parent or sibling, three in Group B lived with parent or sibling, and an additional three of the seven living with husband, wife, son, or daughter, were living in a dependency relationship.

## EVALUATION

### II. Appraisal of Total Sustaining Service

Altogether, 100 patients were in the sustaining service over a period of 2½ years beginning August 13, 1957. Twenty of these were referred from the community. The remaining 80 had been treated in the Crease Clinic or Provincial Mental Hospital during the previous year before coming to the sustaining clinic. These 80 patients had spent a total of 251 years in mental hospital. Up to March 1, 1960, the end of the initial phase of the study, 11 of the 80 patients returned to hospital, four for a period of less than one month. By March 1, 1961, a total of 19 had required admission to hospital for periods ranging from two weeks to one year, and five are currently in hospital.<sup>9</sup> One of the 20 patients from the community required a brief period of treatment (less than one month) in a mental hospital in the 3½ years.

In addition to the 11 patients who returned to hospital by March 1960, 34 patients left the sustaining service (Table V).

TABLE V.—REASONS FOR SEPARATION FROM SUSTAINING SERVICE (34 PATIENTS)

Separation to appropriate community resource . . . . .	18
Attendance interrupted because of conflicting demands . .	6
Patient withdrew, declaring no further need for service . .	5
Patient sought other community psychiatric resource . . .	2
No known reason . . . . .	2
Died . . . . .	1

In the following year, March 1, 1960-March 1, 1961, another six left, and 40 continue to receive service in the clinic, including those who have returned to the Adult Clinic from a mental hospital.

In addition to the improvement associated with the usual methods and procedures designated as therapy, benefit comes to the patient from such factors as identification with the clinic, enthusiasm and persistence of both therapist and patient, emphasized in the latter by long-term voluntary participation, i.e. belonging. This fundamental interchange is either aided or handicapped by the reaction of the community reflected in family attitudes and opportunities for group affiliation.<sup>8</sup>

## CONCLUSIONS

In the total series of 80 patients who had been discharged from hospital in the year prior to the beginning of the study, 13.7% relapsed and were returned to hospital during a follow-up period of 2½ years. After 3½ years, 22% of these 80 patients required hospital admission.

Sustaining service patients responded satisfactorily to the responsibilities of regular attendance on a voluntary basis.

When gains were measured by improved performance, lessened tension, and better ability to form social relationships, a group of 20 sustaining clinic patients showed improvement similar to that of 20 patients given interview therapy.

"Improvement" was most frequently recognized in a lessening of subjective discomfort; next, in an improvement of relations with other people, and last in improved working capacity, in a ratio of 10: 8: 7.

Sustaining service patients relied upon family and financial assistance for support.<sup>10</sup> They were not responsible for family and financial responsibilities.

The residual disability of the group of formerly hospitalized patients was considerable.<sup>1</sup> Rehabilitation did not often extend to gainful employment.

A judgment about success in rehabilitation must be based on the fact that improvement in most cases was neither dramatic nor complete. Three-quarters of patients who had some benefit in any of the three categories were improved by one point only on the rating scale.

A sustaining service requires long-range planning in which provision is made both for regular, continued visits for some patients and assurance of consultative service for those whose supportive care is undertaken elsewhere.<sup>3</sup>

The principal achievement is the establishment of a group of people in the community suffering from a chronic disorder and achieving such a level of support that only a minority will require periodic return to hospital. Until recently such a group of patients might have looked to the hospital as their accustomed domicile with only periodic interludes in the community.

#### SUMMARY

Outpatient aftercare for mental hospital patients includes provision for both an interview service and a sustaining clinic. A sustaining clinic that provided support for a pilot group of 80 patients is described and evaluated. Patients were seen over a period of at least one year, the principal treatment being monthly visits with a psychiatrist or a social worker. Attendance was encouraged at a patients' social club, which met the same evening on the clinic premises. Medication

and specific services were also offered, but no formal psychotherapy, casework, or day-hospital type of program was provided. The purpose of this clinic was to avoid periodic re-admission of the long-term sick, mobilized patient to the mental hospital. A substantial number of patients exceeded the minimum goal and showed significant improvement.

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## CASE REPORTS

### AN UNUSUAL CASE OF CENTRAL RETINAL VEIN OCCLUSION, TREATED SUCCESSFULLY WITH INTRAVENOUS FIBRINOLYSIN\*

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OCCLUSION of the central retinal vein (C.R.V.) is an ocular emergency which has had a bad prognosis in the past. In 10-20% of cases with complete occlusion of the C.R.V. intractable secondary hemorrhagic glaucoma develops in three to six months. Ultimately, 20% of those less than 50 years of age obtain 20/30 vision, and 50% have less than 20/400 vision.<sup>1</sup> Anticoagulant therapy has been tried, but the final results in terms of useful vision do not seem to be better than those in untreated cases.<sup>2</sup> In recent years intravenous infusion of fibrinolytic (human) has been used in the treatment of C.R.V. occlusion, with some evidence of success. Fibrinolysin is a proteolytic and fibrinolytic enzyme of human blood, present in the inactive form as plasminogen. In the case presented, "Lyovac Throm-

bolysin",®\* a commercial preparation of human fibrinolysin, was employed. This agent is prepared by activation of the human blood plasma fraction, plasminogen. Pooled blood plasma is fractionated by the Cohn cold ethanol procedure,<sup>3</sup> and the plasminogen is separated by fractional extraction. It is then heated for 10 hours at 60° C., and activated by purified pyrogen-free streptokinase to yield fibrinolysin which exhibits both profibrinolysin-activator and fibrinolytic properties. Each unit of Thrombolysin® is the amount that will produce lysis of a standard fibrin clot in 10 minutes under standard conditions of pH, temperature and concentration.<sup>4</sup>

#### CASE HISTORY

T.W., a 72-year-old white woman, was admitted to the ophthalmology service of the Royal Victoria Hospital, Montreal, on April 17, 1961. One week before admission she complained of painless blurred vision in the right eye upon arising. She noted no pain and no alteration in her vision in the ensuing week and concluded that her glasses were at fault.

The functional inquiry was unremarkable. Her history of previous illnesses revealed that in 1941 she was admitted to the Royal Victoria Hospital with a diagnosis of chronic septic tonsillitis which was treated by tonsillectomy. In 1954 she was again admitted with an incomplete sacro-pubic hernia which was repaired

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by an anterior and posterior herniorrhaphy. In 1956 she had an excision of a cornu cutaneum and senile keratosis of the upper lip, and in 1960 a basal cell carcinoma on the left chin was excised. On physical examination she was an obese, healthy-appearing elderly woman, very alert for her age. There were no abnormalities of the head and neck. The respiratory system was normal to auscultation and percussion. The blood pressure was 175/95, the heart rate was irregular at 80/min., and a loud harsh precordial systolic murmur was noted, which was loudest in the aortic area. The breasts were normal. The abdomen was obese but was not tender to palpation, and no masses or organs were palpable. The extremities were examined; there was no pitting edema or deformity; the peripheral pulses were present and bilaterally symmetrical. Examination of the central nervous system produced no evidence of abnormality or dysfunction.

The ocular findings were as follows. The patient's visual acuity with glasses was 20/400 in the right eye and 20/60 in the left eye. The ocular tension in the left eye was 21.0 mm. Hg and 18.5 mm. Hg in the right eye. External inspection showed that the lids and conjunctiva were unremarkable and the motility was normal. The slitlamp examination of both eyes revealed cornea that were not unusual for the patient's age, with bilateral arcus senilis only. The anterior chambers were clear of cells and flare, and were of normal depth. Each iris showed mild degenerative changes and the pupils were circular, 3 mm. in diameter, and reactive to light. The lens showed early nuclear sclerosis with some peripheral subcapsular changes. The vitreous had minor degenerative changes with slightly increased fluidity, and increased fibrillar and conglomerate particulate matter. Examination of the fundus of the right eye revealed numerous flame-shaped and blotchy hemorrhages throughout the entire retina. The veins were grossly dilated and the arterioles full. The macula was obscured by hemorrhages and this disc was noticeably paler than the left. The disc of the left eye appeared normal. The macula showed slight granularity and increased pigmentation; there was no foveal reflex present. The vessels showed Grade II arteriosclerosis. The venules were unremarkable. There were no hemorrhages, but small posterior pole Drusen bodies were numerous. Gonioscopy indicated that the angles of the anterior chamber of each eye were wide open.

The provisional diagnoses in this patient were: (1) endogenous obesity, (2) arteriosclerotic heart disease (Grade IV, Class D), (3) central retinal vein occlusion in the right eye, (4) senile macular degeneration in the left eye, (5) mild diabetes mellitus.

The following laboratory data were recorded. A urinalysis showed a negative test for albumin and a 1+ test for glucose. The hemoglobin was 15.5 g. or 99%, the hematocrit 49%; the leukocyte count was 9200 with a differential of bands 1656, mature neutrophils 6164, basophils 92, eosinophils 92, monocytes 276 and lymphocytes 920. The mean corpuscular hemoglobin concentration (M.C.H.C.) was 31% and the erythrocyte sedimentation rate (E.S.R.) was 9 mm. in 1 hr. A blood film showed that the platelets were abundant. The bleeding time was 5 min., the clotting time was 16 min., the prothrombin time was 13 min. with a control of 11.5 min.; and the prothrombin activity was 100%. The nonprotein nitrogen was 24 mg. %. The blood sugar level before a meal was 101 mg. % and the postcibal concentration was 112 mg. %.

#### *Treatment and Progress*

The patient was treated with 100,000 units of human fibrinolysin in 500 c.c. of 5% glucose and water. Anticoagulant therapy was begun with hydroxycoumarin (Marcumar), 18 mg. orally with appropriate dosage thereafter according to the prothrombin estimations. On April 18, the patient noted a subjective improvement in vision, which on objective measurement was 20/100, in the right eye. Another 100,000 units of fibrinolysin was administered that morning and a further 100,000 units in the afternoon. On April 19, visual acuity of the right eye was 20/80 and a further 200,000 units of fibrinolysin was given. She was maintained on a therapeutic dose of hydroxycoumarin (Marcumar) and was discharged on April 22, 1961, with visual acuity of 20/50 in the right eye and 20/60 in the left. At the time of discharge from hospital the hemorrhages were clearing but numerous yellow exudates remained. The patient continued on anticoagulant therapy as an outpatient. On May 4, 1961, the patient returned to the ophthalmology department of the Royal Victoria Hospital with the complaint of awakening that morning to find that the vision in her right eye had deteriorated once more, although she was considered to be under adequate anticoagulant therapy at that time. Central retinal vein occlusion was present in the right eye for the second time.

The ocular findings were as follows: visual acuity with glasses, right eye 20/400, left eye 20/80. The tension in the right eye was 21.0 mm. Hg and in the left 18.5 mm. Hg. The results of slit lamp examination were similar to those reported in April. Fundusoscopic examination on the right showed a disc which was slightly pale; the macula was obscured by hemorrhages and the retinal arterioles were full and showed Grade II sclerosis; the venules were dilated and engorged; many flame-shaped hemorrhages were noted throughout the entire retina but these were most marked along the inferior temporal and inferior nasal venules. Numerous Drusen bodies and exudates were visible. The left eye was unchanged from the April examination.

The laboratory investigation included: a urinalysis with a specific gravity of 1.018, an absence of protein, a 1+ glucose and a microscopic examination which showed 1-3 white blood cells per high-power field, many hemogranular casts and numerous epithelial cells.

The results of biochemical investigations were as follows: the serum uric acid was 5.9 mg. % and the nonprotein nitrogen 26 mg. %; the total proteins were 6.9 mg. % with an albumin fraction of 3.5 mg. % and a globulin of 3.4 mg. %; the serum cholesterol was 289 mg. % and the blood sugar values were 122 mg. before breakfast and 138 mg. after the meal; the serum alkaline phosphatase was 9.1 units; serum potassium and calcium were 4.4 and 5.13 mEq./l. respectively.

Other laboratory results were: hemoglobin 14.7 g. %; hematocrit 47%; M.C.H.C. 31%; the leukocyte count was 19,000 with a differential count of bands 2470, mature neutrophils 13,680, basophils 190, monocytes 1520 and lymphocytes 1140; the reticulocyte count was 1.5% and the E.S.R. 15 mm. in 1 hr.; the platelets were abundant on the blood film. Separation of the serum proteins by electrophoresis gave these results: total proteins 7.94 g. %, albumins 5.94 g. %, alpha<sub>1</sub> globulin 0.44 g. %, alpha<sub>2</sub> globulin 0.96 g. %, beta globulin 0.92 g. % and gamma globulin 1.44 g. %.

The advisability of administering a second course of fibrinolysin, which acts as a foreign antibody-

producing material, was given serious consideration. In order to reduce the possibility of an anaphylactoid reaction, 50 mg. of hydrocortisone (Solu-Cortef) was given intramuscularly and 50,000 units of fibrinolysin was started in 250 c.c. of 5% glucose and water; 20 mg. of hydrocortisone was added to each fibrinolysin infusion. The prothrombin time, prothrombin activity and lysis time were determined every hour for the duration of the fibrinolysin infusion. The time required for the infusion was 10 hours, during which 500,000 units of fibrinolysin were administered. On the morning of May 5, the patient had some flushing of the face and neck and complained of a stiff right arm and knee. At this time her visual acuity with glasses was 20/80 in the right eye and 20/80 in the left. The patient was given a 1200-calorie diabetic diet of 70 g. protein, 50 g. fat and 150 g. of carbohydrate, and was continued on anticoagulant therapy. On May 8, her visual acuity with glasses was 20/70 in the right eye and 20/70 in the left eye and she was able to see the numerals on her wristwatch well enough to "tell time". The patient was discharged May 13, 1961, when her visual acuity with glasses was 20/40 in the right eye and 20/60 in the left.

She has been followed in our outpatient clinic since that date; the hemorrhages and exudates continue to clear although many of the latter are still present; the vein is now completely patent.

#### DISCUSSION

This 72-year-old housewife had an occlusion of the right central retinal vein which was successfully treated with fibrinolysin and anticoagulant drugs on her first admission. However, while the patient was maintained on adequate anticoagulant therapy on an outpatient basis she suffered a second occlusion of the right C.R.V. This occlusion became

patent after the administration of a second course of intravenous human fibrinolysin.

The factors involved in using doses of a foreign protein after an initial sensitizing dose must be weighed carefully; in this case, as in all cases of central retinal vein occlusion, the grave prognosis justifies the acceptance of this degree of calculated risk. To decrease the probability of the development of an anaphylactic response, prophylactic hydrocortisone was administered. Fibrinolysin in the amount of 250,000 units was administered before the lysis time was increased sufficiently to produce effective dissolution of the clot; the patient developed a detectable antithrombolysin titre following the administration of fibrinolysin on April 17, and 250,000 additional units were required to overcome this development.

Our experience with this patient, like that of other authors, supports the opinion that human fibrinolysin is an effective agent in the treatment of central retinal vein occlusion.<sup>5</sup> This appears to be the best therapy available at the present time. Its action is specific on fibrin and does not appear to alter other plasma proteins; the side effects appear to be minimal.

The authors wish to thank Merck, Sharp & Dohme Pharmaceutical Co., who supplied the fibrinolysin in the form of "Lyovac Thrombolysin"® for this patient, and Dr. Alan Kendall of the Anticoagulant Service, Royal Victoria Hospital, who supervised the anticoagulant therapy.

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### UNINTENTIONAL HYPOTHERMIA\*

E. S. RUSSELL, B.A., M.D.,  
Kingston, Ont.

DURING Canadian winters people who break through ice or get lost in woods, etc., suffer from varying degrees of exposure. Most of these are treated in homes or offices, so that accurate observations of such patients' condition and response to treatment are seldom recorded. This report has to do with such a case of exposure in which the patient was seen in hospital.

On a cold winter day J.D., a normal 4-year-old white boy, went out to play. Some time during the morning he fell through the ice into a creek. A 3-year-

old playmate eventually made his way through the snow across a half mile of field to his home and convinced his mother that J.D. had fallen through the ice.

His mother called a neighbour and then hurried to the creek, where she found the boy floating face down. The woman broke through the ice and picked up the child but was unable to free herself from the mud. She stood in the water holding the child until a neighbour returned with a rope and was able to get both to safety.

The child, who had been in the icy water more than half an hour, was then treated in his home with dry clothing, blankets and hot water bottles. After about an hour of such treatment he was moved to hospital.

In the emergency department, the child was found to be comatose, breathing fairly well, cold to touch and shivering vigorously. The heart rate and rhythm were monitored by a cardioscope, an instrument that projects the electrocardiographic pattern to a visual oscilloscope. The pattern was somewhat obscured by

\*From the Department of Anesthesia, Queen's University, Kingston, Ont.

interference due to shivering, but an irregular pulse with bursts of extra systoles, thought to be ventricular in origin, was observed. The rectal temperature was 25° C. (77° F.). Oxygen was given by mask, atropine 0.3 mg. and chlorpromazine 5 mg. were administered intramuscularly and the child was wrapped in regular blankets. A surgeon, a cardiac arrest tray, endotracheal tubes, a gas machine and a supply of warm normal saline were available in the event of cardiac arrest. The shivering was controlled by the 5 mg. of chlorpromazine, and the temperature rose 1° C. in the first half hour, 1.5° C. in the second half hour and 3.5° C. in the third half hour. The child became more responsive and when his temperature reached 31° C. (88° F.) and the pulse was regular, he was transferred to the hospital recovery room. Two hours later his temperature was 37° C. (98.5° F.). The child wanted his mother and appeared none the worse for his adventure.

Urinalysis at that time showed acetone 2+ and glucose 1+. His temperature rose to 40° C. (104° F.) over the next two days and then dropped abruptly to normal. He left the hospital and has remained well.

#### DISCUSSION

Mitscherlich and Mielke,<sup>1</sup> in their book on the Nuremberg medical trial, report that in the experiments with low temperature, danger of death existed at body temperatures below 30° C. (86° F.) and the test persons inevitably died when their body temperature declined to 28° C. (82.5° F.), despite all rescue attempts. They stress the ill effect of cooling the back of the neck (failure of regulatory centres), the rise in blood sugar, and rigor in the muscles. It is further pointed out that strong external heat application is never harmful, and immersion in a hot bath is the best and most useful method of re-warming hypothermic patients. These authors apparently speak with fair authority, as they ran three to four hundred experiments in which 80 or 90 test persons died.

A remarkable case is reported by Laufman<sup>2</sup> concerning a Negress who, in an alcoholic stupor, was brought to hospital with a rectal temperature of 18° C. (64.4° F.). She was slowly re-warmed and managed to survive but suffered severe damage from frost bite to all extremities.

Cooper and Ross,<sup>3</sup> while recognizing the advantages of rapid re-warming, point out the danger to some extremities, their condition being such that rapid heating would lead to extensive gangrene. They also describe effective, slow re-warming in which the body produces sufficient heat to re-warm itself if adequate insulation is provided.

A half-hearted attempt to re-warm by a few hot water bottles is unacceptable. The resultant peripheral vasodilatation, fall in blood pressure and severe "after drop" in deep temperature is described, and may well be fatal. Thus re-warming depends on available facilities and the initial condition of the patient.

This report describes a child who was exposed at 0° C. for probably half an hour and was further kept outside for a similar period in clothes

that were soaked through. It seems likely that sufficient air was trapped in his snow suit to keep him floating and his face was kept out of the water by a piece of ice which he broke from the edge of the hole in the creek. It is not possible to estimate accurately the period of exposure or to guess at his lowest temperature.

The treatment was mostly expectant and, as he had been treated initially by insulating blankets, it was elected to continue slow re-warming. Chlorpromazine controlled the shivering which was contributing to the acidosis and throwing an extra load on the myocardium.<sup>4</sup> The general hypertonicity of muscle is reduced by the direct effect of chlorpromazine on the muscle fibres plus a possible effect on the hypothalamic temperature centre.<sup>5</sup>

Evans and Gray<sup>4</sup> remind us that ventricular fibrillation may occur at any temperature, but it is much more likely with a heart muscle temperature below 29° C. In the case described in this report, such an eventuality was anticipated, and had it occurred, immediate thoracotomy with cardiac massage and copious amounts of warm intrathoracic saline to raise the myocardial temperature would have been used. The essential oxygenation would have been effected by endotracheal oxygen under intermittent positive pressure.

#### SUMMARY

A case of unintentional hypothermia of severe degree, with recovery, is reported. Methods of re-warming patients suffering from exposure, and some of the complications, are mentioned. The plan in this instance, including slow re-warming, administration of chlorpromazine and preparation for possible cardiac arrest, would appear reasonably adequate for such emergency situations.

Gratitude is expressed to S. L. Vandewater, F.R.C.P.[C], Professor of Anesthesia, Queen's University, for constructive advice during the preparation of this report, and to Michael Ryan, M.B., for permission to publish details of his patient.

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## RUMBLES FROM AN OLD VOLCANO

**F**EW subjects are more likely to arouse the ardour and spleen of the physician than the perennial problems of medical education. What the curriculum is to be; the relative merits of the various subjects which compete for time within it; the appropriate time for the introduction of clinical material; the struggle for *Lebensraum* waged by the ancient and previously honoured preclinical subjects; the function, composition and duration of internship; the nature of the contribution of general practitioners to medical education: these and related topics are the foci of "the pent-up dissatisfaction of the profession with its educational system which, every year or two, erupts like a volcano, only to settle again in smouldering and sulky quietness."

In a pungent editorial that should bring forth resounding bravos from all concerned, Osler (*Boston M. Quart.*, 12: 72, 1961) has recently examined the content of such rumblings, disposing of some of them with dispatch, and bringing the reader back to earth with time-honoured and eminently sensible advice. Therein he notes that these periodic eruptions are a good thing and should arouse concern only if they recur without producing change. "The only real enemy is placid acceptance of the status quo. A medical school which pursues its course untroubled by annual doubts about the improvement of its program is already in the death throes. Last year's program should only be the same as this if careful consideration of each hour of the student's time shows no possibility of improvement within present resources. But change for change's sake has nothing to recommend it, and useful experiments with the curriculum demand a sound underlying hypothesis. The tradition of a school is no more than acquired "know-how" handed down from the past. At its best, it is solid, inherited wealth to be preserved at

all costs; at its worst, the dominance of hidebound custom to be discarded at the first possible moment."

Rutstein's concept of separate undergraduate medical courses for the future specialist and the general practitioner is introduced in the terms of the proponent's own definition of the educational needs of each, and closed out with the question "Is there much in the present four-year training curriculum that either could dispense with?" However, Rutstein's proposals (*Lancet*, 1: 489, 1961) deserve close examination by all who are interested in the evolution of medical education. In addition we are told that a startling, if not shocking, thesis was debated before the 57th Annual Congress of Medical Education and Licensure in Chicago earlier this year. The deans of three medical schools and a professor of hospital administration in a fourth school debated the motion: "For graduates of United States Schools, the internship has outlived its educational values and should be discontinued." To this Osler replies, "There is no part of medical training of greater value than the internship, and none more certain to be retained whatever else may go."

In the undergraduate curriculum the fundamental objective of all is that the limited time available be used in the best way possible to provide a foundation for all types of medical practice. In discussing the means currently used to ensure this objective, Osler affirms that teaching at the bedside and in the outpatient department is the rock upon which all clinical education rests, but wonders if the time spent at the bedside is not being gradually whittled away, for often the student himself feels that he has insufficient clinical training. He asks, "Should not his third-year program be brought closer to the fourth? Does he endure too many lectures and see too few patients?" His comments on this are all very well as far as they go, but they seem to assume that all students are alike in the way in which their needs will be satisfied and in the time in which a given experience will be most helpful to them. Good students in their third year at a school where didactic lectures had been almost eliminated have, indeed, requested lectures that would provide a guide to current orthodox views on such massive topics as the etiology of coronary artery disease, for example. The student needs help at every stage in his undergraduate education in the form of a framework around which to organize his new knowledge, but instructors who can provide lectures of this type are always in short supply. Osler properly insists that lectures "if given at all, should be used to teach principles", but goes beyond this, and beyond this writer's concurrence, when he continues "But the truth is, the lecture is a relic of the days when there were no good textbooks." There is, in fact, good reason to believe that those teachers who are satisfied with the texts from which they teach are far outnumbered by

those who are not. Many instructors cannot find a book that presents a given subject as they believe it should be presented at the undergraduate level. The difficulty is that neither the good lecture nor a series of them, nor the good textbook nor a shelf of them, are enough for the student without judicious supplement by an experienced and competent adviser.

The necessity for guidance in the welter of hypotheses, theories, suppositions, facts, "perhaps-facts", opinions, prejudices and ignorance-with-a-thin-veneer-of-jargon, which washes over the student in an unending tide, makes attractive the suggestion of a pattern of tutorial sessions to supplement the lecture course. Osler nominates the resident for a key role in these tutorials on the ground that teaching the subject will reveal to him important gaps in his own knowledge. This is true enough, but teaching by the tutorial and the seminar strains the capacities of even the most devoted teacher. It requires the mastery of a new technique and, if anything, takes more preparation and infinitely more time for evaluation than does the lecture. For each student he has under tutorial or in his seminar the instructor has to keep, in his head usually, a perpetually changing record on which is noted the meandering progress of the student toward understanding. This role requires the skills of the interviewer and considerable patience joined to a palpable enthusiasm for students and for the subject, as well as that rare gift that allows the mentor to help without draining away the tyro's initiative. Academically this demands a comprehensive knowledge not only of the subject under discussion but of the clinical and pre-clinical sciences that border upon it, for despite the desire to keep the topic "on the rails" and the instructor's determination to finish with viral hepatitis by 11 o'clock, the discussion bounds thither and yon. In short, if the tutorial is to be used effectively, tutors will have to be trained, except in that rare school where these valuable people spring unbidden from the cultural soil. The resident, however willing and despite the fact that the process is stimulating for him, should not have this task added to his already considerable load.

Further to the matter of the foundations of clinical training, Osler draws forth a fervent amen with his comment that "the early teaching of the methods of physical examination requires great care and emphasis and should be in the hands of the very best clinicians a school possesses." This is a respected belief, but the best clinicians are already carrying much of the load of instruction in the outpatient department in addition to the multiple and continually proliferating tasks within their respective departments. Thus, this important duty all too often is assigned to an experienced clinician but, by default, passes down to the resident or even to more junior interns.

There is a good deal more in this lively and penetrating disquisition, but part of Osler's summation is worth specific notice:

"We must not be rushed into alterations of our basic system of medical training by the vast accumulation of new medical knowledge. This new knowledge is, I suspect, more of an anxiety to the tutor than the student. I believe the student is perfectly capable of absorbing it for himself, and will do so. What the student *cannot* get, except in his early teaching, are the techniques of his clinical work, for they cannot be learned from books. Let us concentrate, then, on this task of showing him how to examine, diagnose, and treat. And let us remember that the function of an undergraduate medical school is to produce, after five years of training, a doctor who can safely be licensed to practice in the community. The medical school is *not* a place where facts needed by every conceivable type of scientist or specialist are poured into students. It is an environment—a part of a university, in which, by observation of others, by personal study of the literature, by experiment, and by practice with patients, a student may acquire for himself the basic skills and principles needed to practice in a learned profession. He must get first things first. Both the would-be general practitioner and future specialist need these first things; there is no short cut. Then, later, both will build on a solid foundation for the rest of their lives."

#### THE VACUUM EXTRACTOR—A USEFUL OBSTETRICAL INSTRUMENT

THERE has long been a need for an obstetrical instrument which may be used when forceps are contraindicated and Cesarean sections are undesirable. The Malmström vacuum extractor appears to meet this need.

Prior to the introduction of this comparatively new instrument, many Cesarean sections, Dührsen's incisions or difficult forceps deliveries were carried out in the face of incomplete dilatation of the cervix, because of fetal distress, incoordinated uterine action or failure of progression of labour. This vacuum extractor, or "ventouse", appears to be a useful adjunct in the management of such cases, in which it simply hastens delivery through the normal application of the vertex against the cervix without causing any increased risk to the mother or the infant. Its very safety is inherent in two simple facts: (1) if the instrument is wrongly applied, so that the cervix, vagina or membranes are caught within the suction cup, the instrument disengages itself, because these intervening parts prevent the creation of a vacuum; and (2) if disproportion is encountered, the same safety measure is introduced. It is fundamentally impossible to apply the same amount of traction with the vacuum extractor as one might apply with forceps. Actual experience with the vacuum extractor confirms the

belief that less knowledge and skill are necessary with this device than with any obstetrical forceps.

The disadvantages are that it is necessary to apply the suction over a certain period of time, usually for about five to ten minutes; that it is a relatively new and therefore unfamiliar instrument; and that its cost is considerably greater than that of any obstetrical forceps. The extractor is equipped with three sizes of vacuum cups, and before it can be applied it is necessary that the cervix be dilated at least to the extent that it will accommodate the smallest of these cups. The membranes must be ruptured and, as in all cases, an accurate knowledge of the presenting part is essential. The instrument should never be applied to a face presentation, and there is some question whether a breech presentation should be delivered as such, by this means.

A recent survey of retinal hemorrhages which were encountered in newborn infants indicated that these occurred with no greater frequency among infants delivered by the vacuum extractor than among those born by spontaneous delivery. The rare occurrence of abrasion or cephalohematoma is a low price to pay for avoiding vaginal or cervical lacerations, disfiguring forceps marks and Cesarean sections. The incidence of these complications of delivery with the vacuum extractor is usually considerably less than 5%, and no permanent damage has yet been reported.

In general, the indications for use of the vacuum extractor are similar to those for the use of obstetrical forceps. These include the presence of fetal distress, inadequate uterine contractions or inertia and certain other causes of delay in the progression of labour. Lack of skill and experience in the use of obstetrical forceps is a further indication for employment of the vacuum extractor. This instrument also appears to be of value in the rotation of occiput posterior positions, and in the presence of low and high transverse arrests, and slight or moderate asynchronism.

A decrease in the incidence of episiotomy extensions and an absence of cervical lacerations have been consistently noted by those who have reported their experiences with this instrument.

It has been suggested by some that the order of preference for the management of vertex deliveries should be as follows: (1) spontaneous delivery, (2) low forceps delivery, (3) vacuum extractor delivery, (4) mid-forceps deliveries and rotations and (5) Cesarean sections.

In the light of the experience with this device that has accumulated over the past ten years it appears reasonable to state that the Malmström vacuum extractor should be available in every delivery room and that every physician who practises obstetrics should be familiar with its use and indications.

W.F.B.

## A CENTRAL REGISTRY FOR HUNTINGTON'S CHOREA IN CANADA

**H**UNTINGTON'S chorea is a relatively rare disease, but because of its hereditary characteristics and the fact that it usually leads to some mental disturbance, it presents moral, economic and social problems of considerable magnitude. The origins of most of the afflicted families in the United States are fairly well known as a result of studies covering a period of over 300 years which indicate that the hereditary stream of the majority of American cases of Huntington's chorea had its source in certain regions of southern England. Unfortunately, no such study has been completed in Canada. Some years ago Dr. J. P. S. Cathcart, in Ottawa, initiated a register of all cases of this disease among Canada's veterans of the two world wars and among their civilian relatives. For many years Dr. C. H. Archibald, his assistant, gathered from across Canada a considerable number of histories and pedigrees of this group of patients. This register was maintained until 1951, when Dr. Cathcart retired as Chief Neuropsychiatrist of the Department of Pensions and National Health. Upon his retirement he turned over these confidential files to Dr. C. G. Stogdill, of the Department of National Health and Welfare. Since then the register has been studied by Professor F. R. Wake. Through his courtesy and with the permission of Drs. Cathcart and M. Martin, Chief, Mental Health Division of the Department of National Health and Welfare, Ottawa, the complete files and charts have been transferred to Dr. André Barbeau, Director, *Centre de Neurogénétique*, University of Montreal.

Plans are now in progress to establish a Central Registry to classify and study all cases of Huntington's chorea across Canada. This registry now contains over 150 kinships of Canadian families. Physicians and medical administrators throughout the country are urged to communicate with Dr. Barbeau to report new cases and to exchange information concerning patients and their relatives. Such information will be of considerable value in facilitating the planning of more effective research and in co-ordinating the programs of various agencies concerned with the relief of victims of this distressing malady.

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## PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

It is impossible at this date to estimate the number of students who will enter the study of medicine this autumn. With the rapid growth of population in this country and the increasing demand for medical practitioners, particularly in our north-west provinces, our schools have grown progressively in numbers, and classes of large size will no doubt continue.—*Canad. M. A. J.*, 1: 987, 1911.

## Letter to the Journal

### PROVINCIAL MEDICAL LICENSING

To the Editor:

I would appreciate your publishing my letter in the Journal and I hope that the subject may be discussed at a council meeting. I also hope that members of the Association will write their opinions on this subject.

Dr. Roddick, 50 years ago, advocated that every practising physician in Canada, in good standing with the College of Physicians and Surgeons of the province in which he resides and holding a Dominion Council Certificate, should be allowed to practise in any province he desires. The physicians of the Medical Councils should be the first to show consideration to any member of the profession who has the necessity to move to another province. They should try to remove any obstacle which might hinder the physician from serving the community. Instead, however, the medical council of some of the provinces try their best to prevent a confrère from entering their province. While they claim that they are interested in protecting the public, they fail to show a little nobility in helping a colleague to establish himself.

After 28 years of practice in Montreal and for as many years a member of the College of Physicians and Surgeons and other medical societies, holding a C.M.C. certificate, registered to practise in the U.S.A., Latin America and France, I am refused registration in British Columbia. I have a Ph.G., B.Sc. and M.D. degrees and many postgraduate certificates from England, the U.S.A. and France. I have written a good number of scientific papers, yet I am asked to pass an examination in basic science, or else! They imply that there are too many doctors in the province, while the Dean of the Medical School is crying the opposite, asking the government to subsidize medical students to help relieve the shortage! A member of the council said, after I brought the Dean's request to his attention,

"The Dean thinks of himself, we of ourselves." So it is *not* the public welfare they are protecting after all. The average physician in Victoria is overworked and would welcome incoming physicians. Indeed they are even concerned about the unjust obstacles of the College of Physicians of the province, but they are afraid to speak up. The hospitals are overcrowded because the physicians have no time to make home calls, so that patients are asked to enter the hospital if they are not well enough to go to the office. It is unbelievable but true.

A physician not being a member of the B.C. Division of the C.M.A. is *not* allowed into the Sancta Sanctorum of the scientific society meetings. I have travelled all over the world, from darkest Africa to enlightened France, and have attended scientific meetings with an extended courtesy that befits our profession. I have *implored* on several occasions, for the last 1½ years, to be allowed to attend medical conferences, with flat refusal.

I believe that only the parent body of the C.M.A. could undertake to correct such an intolerable situation in the profession. I do not deny that a registration body serves a purpose, but it should not lack common sense and decency to oust fully qualified physicians in excellent standing, because of general rules that seem to serve a selfish end.

I think it is a worth-while matter for discussion. The C.M.A. will deserve the appreciation of the entire profession by solving this problem for the good of all its members. It is not a personal problem. Many have suffered and are uneasy. It is time for our leaders to awaken before it becomes too late and the government will settle the problem.

P. BEREGOFF-GILLOW, M.D.

"Chez Nous",  
3295 Beach Drive,  
Oak Bay, B.C.

## MEDICAL NEWS IN BRIEF

### PRESERVED INTERVERTEBRAL SPACING ASSOCIATED WITH INTERVERTEBRAL DISC DESTRUCTION

In a case report by Caldwell (*J. A. M. A.*, 176: 444, 1961) a 39-year-old man was admitted to hospital with extensive vertebral and paravertebral tuberculosis. A chest radiograph did not reveal evidence of pulmonary inflammatory disease, but huge bilateral paraspinal masses and intervertebral disc-space narrowing in the thoracolumbar area were readily apparent. Numerous vertebrae showed destructive and reparative changes. Plain films of the lumbar spine failed to show disc-space narrowing at this level, but later contrast

studies (obtained by injecting 50% sodium diatrizoate [Hypaque Sodium] into a draining fistulous tract opening in the right lower quadrant) showed complete destruction of the L<sub>5</sub>-S<sub>1</sub> intervertebral disc.

Although in the great majority of cases significant disc disease is associated with disc-space narrowing, this case demonstrates that this association need not necessarily be present. With destruction or alteration of intervertebral discs, the zygapophyseal joints undoubtedly play a major role in, and perhaps the intervertebral ligaments contribute some support to, the maintenance of the disc spaces. It is not certain why these joints and ligaments do not preserve the disc spaces with the more usual degenerative or traumatic disc disease and the typical cases of Pott's disease.

### THE UTILIZATION OF INJECTED VITAMIN B<sub>12</sub> IN MAN

The therapeutic effect, utilization and fate of injected vitamin B<sub>12</sub> in man has recently been the subject of a preliminary report by Adams (*Brit. M. J.*, 1: 1735, 1961). It had been noted, during studies on utilization of injected vitamin B<sub>12</sub> in man, that an injection of 1000 µg. of vitamin B<sub>12</sub> given intramuscularly could not maintain the serum vitamin B<sub>12</sub> level above the pre-injection level, or above the lower limit of normal, for much longer than an injection of 50 or 100 µg. given intramuscularly. It seemed likely that this might be due simply to the increased amount excreted after the larger injection. Detailed investigations, however, have shown that this is not the case and the duration of effect of a large dose of vitamin B<sub>12</sub> is much less than might be expected from the duration of effect of a small dose, even when allowance is made for the amounts excreted after injection. Adams reports observations made on six patients with proven Addisonian pernicious anemia. Large injections—1000 µg.—of vitamin B<sub>12</sub> did not have the expected effect in maintaining the serum vitamin B<sub>12</sub> levels above the lower limit of normal as compared with the effect of small (50 or 100 µg.) injections of vitamin B<sub>12</sub>. This phenomenon is not due to the larger amount excreted after the 1000-µg. injection, and it is possible that, in the case of the larger injection at least, some of the injected vitamin B<sub>12</sub> may be inactivated in the body. From the results it appears that 100 µg. intramuscularly every three to five weeks is the most economical and effective form of maintenance therapy in patients with pernicious anemia.

### ALLERGIC VASCULAR REACTIONS DUE TO TOBACCO

Tobacco allergy was investigated in 72 healthy smokers, some of whom had previously shown various allergic disorders, and in eight smokers with vascular disorders: two cases of migratory thrombophlebitis, two cases of superficial thrombophlebitis, three cases of thromboangiitis obliterans, and one case of obliterating arteriolitis involving the superficial cutaneous vessels. Investigations by Longhin, Popescu and Trifu (*Rumanian M. Rev.*, 4: 55, Oct.-Dec., 1960) included scratch tests and intradermal tests with a tobacco extract prepared according to Sheldon's method. Tests were positive in 14 (20%) of the 72 healthy smokers, and passive transfer from eight of the 14 sensitive individuals demonstrated the presence of specific reagins. In all of the patients with vascular disorders, all of whom were men and all of whom were "old" smokers (14 to 25 years), the intradermal test with tobacco extract resulted in immediate positive reactions. When smoking was discontinued, the vascular disturbances greatly improved, and as soon as smoking was started again by some of the patients, the lesions reappeared.

Histological preparations revealed the dependence of the pathological response on the structure and physiology of the blood vessel affected. The large deep vessels exhibited thrombosis, fibrinoid degeneration of the media, alterations of the elastic component and perivascular and intramural inflammatory infiltration. The small blood vessels and capillaries, both deep and superficial, showed a process of stenosing, rarely

obliterating, endotheliitis due to proliferation and deformities of the endothelial cells, and a predominantly granulocytic perivascular inflammatory infiltrate with leukocytoclasia and interstitial blood extravasation.

It would appear that tobacco allergy is the primary etiological factor in certain vascular disorders in persons with a specific vascular shock tissue. Its diagnosis in incipient vascular lesions of the superficial or migratory thrombophlebitis type is, therefore, of great importance, as discontinuance of smoking at this time may prevent the appearance of severe vasculitis of the thromboangiitis obliterans type.

### INTRAVENOUS FAT EMULSIONS

When intestinal absorption is impaired for any length of time the physician is faced with the problem of supplying an adequate caloric intake by parenteral means. In recent years fat emulsions have been tried for this purpose, because they eliminate certain disadvantages of other intravenous preparations. Fat does not alter osmotic pressure, it is metabolized without formation of any toxic substances, and feedings can be given in a comparatively small volume of fluid because of the high caloric value of fat.

Vegetable oils have been found more suitable than animal fat because of their high content of unsaturated fatty acids and their lower melting point. They must be purified several times to remove protein, phospholipids and other substances, for these can give rise to untoward side effects. The size of the fat particles must be under 1µ to avoid fat embolism.

A study of intravenous feeding using fat emulsions has recently been reported by Edgren (*Deutsche med. Wchnschr.*, 86: 701, 1961). The first emulsion tried at the Karolinska Institute at Stockholm, Sweden, consisted of cottonseed oil, purified phosphatides from soybeans and isotonic glucose solution. It caused febrile reactions in patients and was toxic to animals when used in amounts supplying more than 50% of their caloric needs. The author then used an emulsion containing a triglyceride from soybeans, egg lecithin as an emulsifier and isotonic glycerine solution as a watery base. This preparation was given to rats in a dose of 12 g. per kg. of body weight for 33 days, and no toxic effects were observed. In 200 surgical patients, it was used without side reactions.

The question has been raised whether fat administered intravenously is actually metabolized by the body, and it has been studied by tagging the fatty acids with radioactive carbon. Most of the fat is taken up by the liver and presumably metabolized there. Two g. of emulsified fat per kg. of body weight was given without liver damage. This amount provides 50% of the caloric requirements. When 6 g. per kg. of body weight was given to dogs, severe liver damage developed. It is therefore important that liver function tests be carried out before commencing therapy.

When fat emulsions were first used, serious side effects such as chills, fever, nausea, vomiting, joint pains, tightness in the chest and dyspnea were seen. These were probably caused by improper purification and were not encountered when the preparation described above was used by the author.

(Continued on advertising page 38)

## ASSOCIATION NOTES

### GENERAL HOSPITALS IN CANADA APPROVED BY THE CANADIAN MEDICAL ASSOCIATION FOR JUNIOR (1ST YEAR) INTERN TRAINING

Name of hospital	Location	Beds (exclud- ing bas- sine-ts)	Teaching beds					Non- teaching beds	Univer- sity affilia- tion**	Number of junior interns accepted	Monthly stipend
			(Public, private and semi-private beds)								
			Medi- cine	Surgey	Obste- trics	Pedia- trics	Other				
<b>British Columbia</b>											
Royal Columbian Hospital	New Westminster	434	162	164	48	48	12	—	no	12	\$200
St. Paul's Hospital	Vancouver	551	80	123	54	57	175	62	U.B.C.	20	190
St. Vincent's Hospital	Vancouver	193	36	36	30	30	—	61	no	4	200
Vancouver General Hospital	Vancouver	1498	126	160	40	175	225	777	U.B.C.	54	163
Royal Jubilee Hospital	Victoria	446	71	59	62	42	—	212	no	8	175***
St. Joseph's Hospital	Victoria	435	160	139	40	71	25	—	no	8	175***
<b>Alberta</b>											
Calgary General Hospital*	Calgary	743	266	280	59	84	20	—	no	20	100
Holy Cross Hospital	Calgary	342	86	107	53	50	46	—	no	8	100***
Edmonton General Hospital	Edmonton	371	124	140	47	50	—	—	U.A.	10	125
Misericordia Hospital	Edmonton	342	117	122	53	50	—	—	U.A.	8	100***
Royal Alexandra Hospital	Edmonton	729	166	109	134	115	205	—	U.A.	18	150
University of Alberta Hospital	Edmonton	1147	303	366	60	128	290	—	U.A.	32	155
<b>Saskatchewan</b>											
Regina General Hospital	Regina	740	175	290	53	140	82	—	no	12	150
Regina Grey Nuns' Hospital	Regina	469	117	225	43	50	34	—	no	20	200
St. Paul's Hospital*	Saskatoon	277	105	116	24	32	—	—	U.S.	7	225
Saskatoon City Hospital*	Saskatoon	349	113	110	31	36	22	37	U.S.	12	240
University Hospital	Saskatoon	530	137	185	37	69	102	—	U.S.	16	125
<b>Manitoba</b>											
St. Boniface General Hospital*	St. Boniface	655	206	316	46	87	—	226	U.M.	26	110
Grace Hospital	Winnipeg	240	32	46	26	6	—	130	U.M.	6	200
Misericordia Hospital	Winnipeg	410	125	185	55	45	—	—	no	8	150
Winnipeg General Hospital*	Winnipeg	831	162	246	106	32	285	—	U.M.	32	110
<b>Ontario</b>											
Brantford General Hospital	Brantford	502	265	141	37	59	—	—	no	6	150
McKellar General Hospital	Fort William	426	83	69	26	50	66	132	no	12	175
Hamilton General Hospital	Hamilton	1160	166	200	86	103	54	551	no	26	175
St. Joseph's Hospital	Hamilton	457	44	46	26	30	72	239	no	12	175
Hôtel-Dieu Hospital*	Kingston	293	136	91	32	34	—	—	Q.U.	11	200***
Kingston General Hospital	Kingston	502	146	189	45	82	40	—	Q.U.	20	150
Kitchener-Waterloo Hospital	Kitchener	436	38	34	24	58	110	172	no	9	250
St. Joseph's Hospital	London	502	78	80	18	42	20	264	W.O.	17	150***
Victoria Hospital	London	884	71	72	15	120	30	576	W.O.	30	150***
Oshawa General Hospital	Oshawa	350	87	70	67	51	75	—	no	12	250†
Ottawa Civic Hospital	Ottawa	873	190	210	78	84	28	283	U.O.	25	150***
Ottawa General Hospital	Ottawa	617	220	combined	24	86	14	273	U.O.	16	175
Hôpital St-Louis-Marie de Montfort	Ottawa	229	27	27	31	45	8	91	no	6	150
Peterborough Civic Hospital	Peterborough	373	138	122	46	41	26	—	no	6	200
General Hospital of Port Arthur	Port Arthur	282	190	combined	28	30	34	—	no	4	245
St. Joseph's General Hospital	Port Arthur	210	68	60	22	60	—	—	no	6	250
St. Catharines General Hospital	St. Catharines	360	94	108	30	50	78	—	W.O.	6-8	250
St. Thomas-Elgin Hospital	St. Thomas	371	110	84	55	24	84	14	no	6	175
St. Joseph's Hospital	Sarnia	347	56	71	30	21	—	169	no	6	200
Sarnia General Hospital	Sarnia	247	59	117	24	47	—	—	no	6	235
Scarborough General Hospital	Scarborough	340	75	103	77	22	63	—	no	12	150***
Sudbury General Hospital	Sudbury	309	63	70	63	60	53	—	no	8	250
New Mount Sinai Hospital*	Toronto	337	72	108	62	22	36	37	no	20	100***
St. Joseph's Hospital	Toronto	516	91	102	32	79	31	231	no	21	175
St. Michael's Hospital*	Toronto	802	148	173	28	—	65	388	U.T.	32	137
Toronto East General and Orthopaedic Hospital	Toronto	647	168	150	103	46	180	—	no	24	142***
Toronto General Hospital*	Toronto	1204	259	270	44	—	82	549	U.T.	39	138
Toronto Western Hospital*	Toronto	694	136	104	52	14	88	300	U.T.	30	150
Wellesley Hospital	Toronto	285	77	83	35	—	40	50	U.T.	9	137
Women's College Hospital*	Toronto	286	97	45	82	4	58	—	U.T.	6	75***
Grace Hospital	Windsor	207	19	25	21	35	—	107	no	4	300
Hôtel-Dieu of St. Joseph	Windsor	382	112	140	53	67	10	—	no	8	300
Metropolitan General Hospital	Windsor	311	85	85	28	42	71	—	W.O.	4	300
<b>Quebec</b>											
Hôtel-Dieu St-Vallier	Chicoutimi	921	264	231	68	214	144	—	U.L.	26	125
Hôpital du Sacré-Cœur	Montreal	735	83	82	55	24	491	—	M.	14	40
Hôpital Saint-Luc	Montreal	414	99	237	35	59	23	—	M.	26	125
Hôtel-Dieu de Montréal*	Montreal	750	107	130	—	—	—	513	M.	22	40
Jewish General Hospital	Montreal	378	53	43	59	29	194	—	McG. U.	16	65***
Maisonneuve Hospital	Montreal	531	312	combined	54	71	94	—	M.	22	65
Montreal General Hospital*	Montreal	729	110	142	40	—	114	323	McG. U.	48	65***
Hôpital Notre-Dame	Montreal	1018	180	180	20	60	—	578	M.	30	65
Queen Elizabeth Hospital*	Montreal	270	107	117	46	—	—	—	McG. U.	9	100
Royal Victoria Hospital*	Montreal	952	189	239	111	49	312	52	McG. U.	32	65***
Reddy Memorial Hospital**** (Westmount)	Montreal	139	26	43	38	4	28	—	McG. U.	7	100***
St. Mary's Hospital	Montreal	301	73	87	37	30	34	40	no	16	150***
Hôpital de l'Enfant-Jésus*	Quebec	521	45	60	53	143	80	140	U.L.	20	100
Hôpital du Saint-Sacrement*	Quebec	286	86	59	—	29	14	88	U.L.	16	75
Hôpital St-François-d'Assise*	Quebec	320	36	42	22	30	60	130	U.L.	9	25
Hôtel-Dieu de Québec*	Quebec	294	26	40	8	10	—	210	U.L.	18-20	25
Jeffrey Hale's Hospital	Quebec	151	51	50	22	28	—	—	U.L.	4	50
Hôpital Général St-Vincent-de-Paul	Sherbrooke	269	36	39	8	38	5	143	U.L. & M.	6	50
Hôtel-Dieu de Sherbrooke	Sherbrooke	332	70	71	20	51	—	120	U.L.	3	75
Sherbrooke Hospital	Sherbrooke	150	54	combined	8	18	—	70	no	6	150
Hôpital St-Joseph	Trois-Rivières	237	10	20	—	34	—	173	U.L.	8	25
Hôpital Général de Verdun	Verdun	420	125	115	42	70	—	68	M.	9	65

Name of hospital	Location	Beds (excluding bassinets)	Teaching beds					Non- teaching beds	Univer- sity affilia- tion**	Number of junior interns accepted	Monthly stipend
			(Public, private and semi-private beds)								
			Medi- cine	Surgery	Obste- trics	Pedia- trics	Other				
New Brunswick											
Victoria Public Hospital	Fredericton	230	60	55	24	32	9	50	D.U.	2	250
The Moncton Hospital	Moncton	302	130	combined	41	45	86	—	D.U.	6	150
Saint John General Hospital	Saint John	522	144	169	65	74	70	—	D.U.	14	100
Nova Scotia											
Halifax Infirmary*	Halifax	223	83	80	60	—	—	—	D.U.	9	75
Victoria General Hospital*	Halifax	558	144	240	—	—	174	—	D.U.	30	100
Newfoundland											
St. John's General Hospital*	St. John's	456	48	108	—	55	191	54	D.U.	15	300***

\*Hospitals having arrangements with other hospitals for part of rotation program.

Parent hospitals	Hospitals supplementing intern training
Calgary General Hospital, Calgary, Alberta	Salvation Army Grace Maternity Hospital, Calgary (Antenatal Clinics)
St. Boniface General Hospital, St. Boniface, Manitoba	Children's Hospital, Winnipeg (Pediatrics)
Winnipeg General Hospital, Winnipeg, Manitoba	Children's Hospital, Winnipeg (Pediatrics)
St. Paul's Hospital, Saskatoon, Sask.	University Hospital, Saskatoon (Psychiatry)
Saskatoon City Hospital, Saskatoon, Sask.	Bethany Salvation Army Hospital, Saskatoon (Obstetrics)
Hôtel-Dieu Hospital, Kingston, Ontario	Ontario Hospital, Kingston (Psychiatry) (Medicine and Surgery)
New Mount Sinai Hospital, Toronto, Ontario	Baycrest Hospital, Toronto (Geriatrics and Chronic Diseases)
St. Michael's Hospital, Toronto, Ontario	Hospital for Sick Children, Toronto (Pediatrics)
Toronto General Hospital, Toronto, Ontario	Hospital for Sick Children, Toronto (Pediatrics)
Toronto Western Hospital, Toronto, Ontario	Hospital for Sick Children, Toronto (Pediatrics)
Women's College Hospital, Toronto, Ontario	Toronto East General and Orthopaedic Hospital, Toronto (Pediatrics)
Hôtel-Dieu de Montréal, Montréal, Quebec	Hôpital Ste-Justine, Montréal (Obstetrics and Pediatrics)
Hôtel-Dieu de Québec, Québec, Quebec	Hôpital de la Misericorde, Québec (Obstetrics)
Hôpital de l'Enfant-Jésus, Québec, Quebec	Hôpital de la Misericorde, Québec (Obstetrics)
Hôpital du Saint-Sacrement, Québec, Quebec	Hôpital St-Michel-Archange, Québec (Neurology and Psychiatry)
Hôpital St-François-d'Assise, Québec, Quebec	Hôpital de la Misericorde, Québec (Obstetrics)
Montreal General Hospital, Montreal, Quebec	Crèche St-Vincent-de-Paul, Québec (Pediatrics)
	Hôpital Ste-Foy, Québec (Medicine and Surgery)
	Hôpital St-Michel-Archange, Québec (Psychiatry and Neurology)
Royal Victoria Hospital, Montreal, Quebec	Catherine Booth Mothers' Hospital, Montreal (Obstetrics)
Queen Elizabeth Hospital, Montreal, Quebec	Montreal Children's Hospital, Montreal (Pediatrics)
Halifax Infirmary, Halifax, Nova Scotia	Charlotte Memorial Hospital, Charlotte, North Carolina (Medicine, Surgery, Obstetrics, Pediatrics)
Victoria General Hospital, Halifax, Nova Scotia	King Edward VII Memorial Hospital, Bermuda (General)
	General Hospital, Sherbrooke (General)
	Montreal Children's Hospital, Montreal (Pediatrics)
	Alexandra Hospital, Montreal (Pediatrics)
	Montreal Children's Hospital, Montreal (Pediatrics)
St. John's General Hospital, St. John's, Newfoundland	The Children's Hospital, Halifax (Pediatrics)
	St. Elizabeth Hospital, North Sydney (Pediatrics)
	The Children's Hospital, Halifax (Pediatrics)
	Grace Maternity Hospital, Halifax (Obstetrics)
	The Moncton Hospital, Moncton, New Brunswick (Pediatrics and Obstetrics)
	Grace Hospital, St. John's (Obstetrics)

\*\*University abbreviations used in list of approved hospitals.

U.B.C.—University of British Columbia  
 U.A. —University of Alberta  
 U.S. —University of Saskatchewan  
 U.M. —University of Manitoba  
 Q.U. —Queen's University  
 W.O. —University of Western Ontario

U.O. —University of Ottawa  
 U.T. —University of Toronto  
 U.L. —Laval University  
 M. —University of Montreal  
 McG. U.—McGill University  
 D.U. —Dalhousie University

\*\*\*Living-out allowance in addition to salary.

\*\*\*\*Credit for additional beds given for Home Care Service.

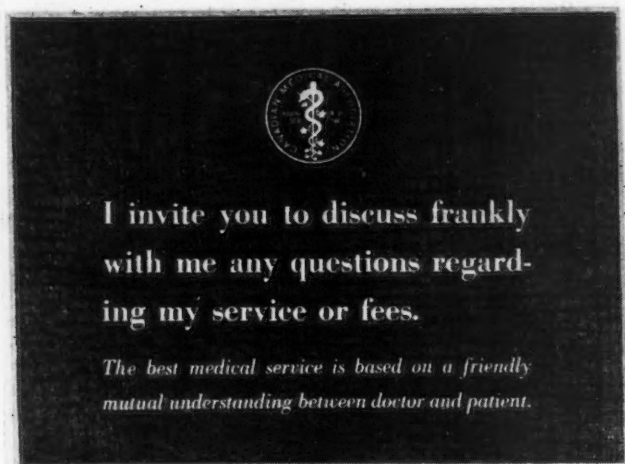
†Canadian graduates, foreign graduates, \$200.

## PR AID FOR DOCTORS' OFFICES

Doctor, would you like to promote better understanding between yourself and your patients?

Patients, in the main, would appreciate an early discussion of fees, and where possible, anticipated hospital and drug costs.

Many doctors find the subject of fees a difficult topic to discuss. Realizing this—and aware that mutual understanding between doctor and patient is essential to good medical service—the Canadian Medical Association's Committee on Public Relations has produced a plaque (see illustration) for use in the doctor's office.



The plaque—in English or in French—measures 9" by 6 $\frac{3}{4}$ ". The wording is printed in gold, on walnut-finish paper fused to heavy  $\frac{1}{8}$ " board. Edges of the plaque are bevelled and gilded. An easel mounted on the back permits it to stand on the desk or to hang on the wall.



Requests for free plaques should be sent to the Secretary of the C.M.A. Division in your area, or to Mr. K. C. Cross, Assistant Secretary, Public Relations, The Canadian Medical Association, 150 St. George Street, Toronto 5, Ont.

## OBITUARIES

### DR. FREEMAN ALBERT BROCKENSHIRE

#### AN APPRECIATION

Dr. Freeman Albert Brockenshire, the son of Franklin S. and Jane Brockenshire, was born near Exeter, Ont., on October 26, 1889, and died in Windsor on July 3, 1961. Shortly after his birth, his family moved to Port Talbot where he received his primary education in a rural school and his secondary education at Dutton High School. He graduated in medicine from the University of Toronto in 1913. He interned in Toronto General Hospital in 1913, Bridgeport, Conn., in 1914, and also at the New York Lying-In Hospital.

During World War I he served with the Canadian Army Medical Corps, going overseas in 1916. He spent three years in France, the first at the front with the Princess Patricia Canadian Light Infantry and the latter part with No. 3 General Hospital at Boulogne.

After the war Dr. Brockenshire returned to Canada as a Major and was posted to Christie St. Hospital in Toronto. After his discharge he pursued postgraduate work in New York.

In 1921 he commenced general practice in Windsor, in which field he practised until 1930. During these years he became intensely interested in orthopedic surgery. He spent considerable time studying orthopedics at Children's Hospital in Detroit. In 1930 he continued further study of this specialty at London, Liverpool and Edinburgh, receiving a fellowship degree in Edinburgh. He furthered his study by visiting other orthopedic centres on the continent. In 1932 he returned to Windsor and was the first doctor to confine his work to the specialty of orthopedics.

Dr. Brockenshire was made an honorary member of the Rotary Club and took an active part in its program on behalf of crippled children. This work he carried on until ill-health compelled him to retire.

He was an active member of the Essex County Medical Society, the Ontario Medical Association, the Canadian Orthopedic Association, and the Windsor Fellowship Society. He served as President of all these organizations. In 1958 he was awarded a Senior Membership in the Canadian Medical Association. Dr. Brockenshire was very interested in the development of the Windsor Medical Services and was its first President in 1939. He also served as President from 1945 to 1950. He served as Chief of Orthopedics in the three Windsor hospitals and was the Honorary Chief of Staff of Hôtel-Dieu.

In 1924 Dr. Brockenshire married Miss Gladys Nicholls. They had two sons, John Hamilton, practising law in Windsor, and Franklin, who died two weeks earlier in a motor accident. One brother, Norman of Talbotville, also survives. To these the Essex County Medical Society extends its deepest sympathy.

Dr. Brockenshire, to those who worked with him and knew him, will be remembered for his keen interest in the progress of organized medicine, both locally and throughout Canada, and for the progress he made in the department of orthopedic surgery.

J.W.B.

## DR. MURRAY SCOTT DOUGLAS

## AN APPRECIATION

The news of the sudden death of Dr. Murray S. Douglas on August 28 came as a shock to his many friends and to the medical profession, not only in his native district but throughout all of Canada. He had stopped in Toronto en route to his summer home at Bear Lake, when he took ill and was admitted to Toronto General Hospital one week before his death.

Dr. Douglas, born at Ilderton on October 7, 1899, was educated in the rural public school, the London Collegiate Institute, and the University of Western Ontario, graduating in medicine in 1922. He acted as an intern in Victoria Hospital during the years of 1921 and 1922. He commenced the practice of medicine in Smooth Rock and Kapuskasing in 1922 and came to Windsor in June 1924, where he carried on general practice with special interest in obstetrics. He became a member of the staffs of Hôtel-Dieu, Grace and Metropolitan General Hospitals, and for 15 years he was chief of the Section of Obstetrics of the Metropolitan General Hospital.

Early in his career in Windsor, he became a member of the Essex County Medical Society and entered enthusiastically into all of its activities. He also belonged to the Ontario Medical Association of which he was the Counsellor of District No. 1 in this organization for some years before he became its President. Later he served with the Canadian Medical Association as Chairman of the General Council and the Executive Committee.

In 1935, the Essex County Medical Society, under the Presidency of Dr. Brockenshire, undertook the study of prepaid medical care. Dr. Douglas was the Secretary of that Committee. In 1937, a charter for "Windsor Medical Services" was procured and this organization came into operation in 1939. He also served on its Board of Directors for a number of years. In June 1959, he was awarded the certificate of the Royal Society of Medicine. He was also a member of the Wayne County Medical Society.

Surviving are his widow, Edith N. Douglas, two sons, Robert George of Hamilton and David Bruce of Windsor, and two brothers Keith and Allan, of Ilderton. To these the members of the Essex County Medical Society, and the medical profession of Canada, extend deepest sympathy.

J.W.B.

DR. CHARLES-ANTOINE GILBERT, aged 59, died August 20, at Notre-Dame Hospital, Montreal. A former student of the Collège de Lévis, Dr. Gilbert received his medical training at Laval University.

He is survived by his widow, two sons and two daughters.

DR. K. G. B. KETCHUM, 59, died August 27, at his home in Waterdown, Ont. Former headmaster of St. Andrew's College, Dr. Ketchum was born in Cobourg, son of Judge Jay Ketchum of Durham county. In addition to his medical degree, Dr. Ketchum held an LL.D. from McMaster University. He was headmaster of St. Andrew's for 25 years, with wartime service as director of studies at the Royal-Canadian Naval College.

Dr. Ketchum is survived by his widow and one son.

DR. C. A. KIRKLAND, minister without portfolio in the Quebec Government, died on August 9, in the Lachine General Hospital. A member of the Legislative Assembly for Jacques Cartier since 1939, Dr. Kirkland was mayor of Ville St. Pierre from 1928 to 1950. Born in St. Constant, Dr. Kirkland was 63 years old. He studied at the Ste. Thérèse and St. John College and obtained his M.D. at the University of Montreal.

Dr. Kirkland is survived by his widow and a daughter.

DR. THOMAS H. MacDONALD, 82, of West Medford, N.S., died August 1. A practising physician for 57 years, Dr. MacDonald was a former staff member of Somerville (Mass.) Hospital, and was also on the staff of the eye and ear infirmary of Massachusetts General Hospital.

He is survived by his widow and a sister.

DR. PETER CRERAR MacINTOSH, 29, died on August 19 in Magog, Que. Dr. MacIntosh was born and educated in Montreal, and received his M.D. from McGill University.

He is survived by his widow and two sons.

DR. A. H. MacNEIL, 81, died August 1, at his home in Briarcrest, Sask. Born in Prince Edward Island, Dr. MacNeil went to Saskatchewan in 1912, and had practised in Shaunavon, Cabri and several other Saskatchewan towns.

He is survived by his widow and three brothers.

DR. ARCHIBALD KITCHENER McNEILL, 61, of Empress, Alta., died at his home recently after a short illness. He was born at Asquith, Sask., and received his early education there. He later attended the University of Saskatchewan and graduated from the medical school at the University of Manitoba.

Dr. McNeill is survived by his widow and three daughters.

DR. JANE SPROULE MANSON, aged 83, died on August 29 in a Toronto hospital. A native of Listowel, Ont., Dr. Manson was one of Canada's pioneer women in the medical field. After graduating in medicine from the University of Toronto, she went on to become Canada's first woman specialist. She took postgraduate studies in Toronto, Vienna and Berlin, and became the first Canadian woman admitted to the Royal College of Physicians in London in 1911. After practising at the Toronto General Hospital, and two years of war service in London, England, she headed the otolaryngology department of the Women's College Hospital.

Dr. Manson's husband, James Manson, predeceased her.

DR. ROGER NADEAU died August 12 in Hôtel-Dieu Hospital, Sherbrooke, Que. Born in Princeville, Que., Dr. Nadeau studied at Nicolet Seminary and at Laval University. Dr. Nadeau served with the Richmond Health Unit and then opened his own office in that community.

He is survived by his widow, a son, and two daughters.

DR. LOUIS S. RUDIN, 69, police court psychiatrist and former assistant medical superintendent at the Oliver Mental Institute, Edmonton, Alta., died August 29. A native of Russia, he came to Canada in 1913 and received his B.A. degree from the University of Manitoba and his medical degree from the University of

Alberta and McGill University.

Dr. Rudin was a former vice-president of the Alberta Psychiatric Association and a former president of the Edmonton Psychiatric Society.

He is survived by his widow, one daughter and two sons.

## ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

### INVITATION TO CERTIFICATED SPECIALISTS OF THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA TO ATTEND THE 1962 ANNUAL MEETING OF THE COLLEGE

In 1959, the College, in keeping with a policy of expanded educational opportunities for Fellows and certificated specialists, embarked on a program of Regional Scientific Meetings, which Fellows and certificated specialists living in the designated region have been invited to attend.

At the 1961 Annual Meeting of the College held in Ottawa, certificated specialists in the immediate local area were invited to attend the scientific program sessions.

Because of the larger meeting-room accommodation available in Toronto, the Council of the College has decided to extend an invitation to all certificated specialists of The Royal College to attend the scientific sessions at the 1962 Annual Meeting, to be held at the Royal York Hotel, Toronto, from January 18 to 20.

Certificated specialists wishing to attend this meeting must complete the attached registration application form and return it to The Secretary, The Royal College of Physicians and Surgeons of Canada, 74 Stanley Avenue, Ottawa 2, Ontario, together with a cheque or money order in payment of the Registration Fee of \$15.00, made payable to the Royal College of Physicians and Surgeons of Canada. In order to facilitate planning for adequate accommodation, registration applications should be forwarded by December 15 at the latest.

A summary of the scientific program will be published in the Journal in mid-December. Certificated specialists who have registered to attend the meeting will also be sent a copy of the printed program at that time.

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The Secretary,  
The Royal College of Physicians and Surgeons of Canada,  
74 Stanley Avenue,  
Ottawa 2, Ontario.

I desire to register to attend the Scientific Sessions of the Annual Meeting of The Royal College of Physicians and Surgeons of Canada to be held at the Royal York Hotel, Toronto, January 18, 19 and 20, 1962.

Enclosed is a cheque/money order in the amount of \$15.00 in payment of the Registration Fee.

Name of Certificant:.....

Address:.....

Name of Specialty:.....  
(please print)

PUBLIC HEALTH

SURVEILLANCE REPORT OF  
EPIDEMIC OR UNUSUAL  
COMMUNICABLE DISEASES

PARALYTIC POLIOMYELITIS

Canada

Seven cases of paralytic poliomyelitis have been reported to the Epidemiology Division during the four-week period from July 9 to August 5, 1961.

The reporting continues at a low level. The provinces of Quebec and Alberta, with 21 and 19 cases respectively, account for 58% of the cases reported in Canada to date.

Only two deaths have occurred so far this year, both in the province of Alberta. For the corresponding period in 1960, 28 deaths had been reported.

The four-week totals (week 28 to week 31) and the cumulative totals to week 31 for the past five years are presented below.

Year	1961	1960	1959	1958	1957
Four-week period, week 28 to week 31..	7	138	315	17	15
Cumulative total to week 31.....	52	389	403	55	61

TETANUS

Two cases of tetanus have been reported from the province of Ontario for the week ending July 8, and one case for the week ending July 22. This last report was of a fatal case in a 9-year-old boy from Lindsay.

PSITTACOSIS

One case of psittacosis has been reported in North York Township, Ont., for the week ending July 29, 1961.

MEASLES

An outbreak of measles on the Montagnais Reserve at Bersimis, Que., was first reported in the surveillance report of June 17. To date there has been a total of 48 cases. No serious complications have resulted and no cases have occurred in those who had received protective doses of gamma globulin.

TRICHINOSIS

Five more cases of trichinosis have been reported in the province of Quebec since July 8, 1961. Three of these cases occurred in Jonquière, one in Arvida and one in Montreal. This brings the total for the year to 53 cases.

INFECTIOUS HEPATITIS

Since the beginning of May, 11 cases of infectious hepatitis have occurred in the Aklavik area of the Northwest Territories.

LEPROSY

One case of leprosy has been reported for the province of Ontario for the week ending July 15, 1961. The patient, a 25-year-old male, has resided in Canada for the past three years. Prior to this time, he had resided for three years in Australia and three years in Malta. Symptoms first appeared last Christmas. Diagnosis has been confirmed by positive smear and biopsy.

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA\*  
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	Week ended (1961):				Cumulative total since beginning of year	
	July 22	July 29	August 5	August 12	1961	1960
Brucellosis (Undulant fever).....(044)	1	4	2	1	76	85
Diarrhea of the newborn, epidemic.....(764)	1	3	—	2	55	34
Diphtheria.....(055)	—	—	—	1	43	20
Dysentery.....(045, 046, 048)	88	76	131	30	1,976	1,794
(a) Amebic.....(046)	—	—	—	—	5	2
(b) Bacillary.....(045)	17	15	21	15	914	1,533
(c) Other and unspecified.....(048)	71	61	110	15	1,057	259
Encephalitis, infectious.....(082.0)	—	1	—	—	1	—
Food poisoning:.....(049.0, 042.1, 049.2)	13	25	17	40	667	866
(a) Staphylococcus intoxication.....(049.0)	—	—	—	—	20	309
(b) Salmonella with food as vehicle of infection.(042.1)	13	23	16	20	619	538
(c) Unspecified.....(049.2)	—	2	1	20	28	19
Hepatitis, infectious (including serum hepatitis).....(092, N998.5)	170	126	152	183	6,518	3,440
Meningitis, viral or aseptic.....(080.2, 082.1)	8	3	12	12	134	362
(a) Due to poliovirus.....	1	—	6	2	15	194
(b) Due to Coxsackie virus.....	—	—	—	4	9	67
(c) Due to ECHO virus.....	—	—	—	—	—	4
(d) Other and unspecified.....	7	3	6	6	110	97
Meningococcal infections.....(057)	2	1	1	—	78	113
Pemphigus neonatorum (Impetigo of the newborn)..(766)	—	—	—	—	9	7
Pertussis (Whooping cough).....(056)	56	52	73	76	2,510	3,431
Poliomyelitis, paralytic.....(080.0, 080.1)	2	2	5	7	60	387
Scarlet fever and Streptococcal sore throat....(050, 051)	83	108	91	89	9,223	16,433
Typhoid and Paratyphoid fever.....(040; 041)	4	5	1	3	157	210
Venereal diseases:.....(020-039)	291	304	467	391	10,941	10,489
(a) Gonorrhea.....(030-035)	239	262	419	351	9,585	9,282
(b) Syphilis.....(020-029)	52	42	48	40	1,355	1,204
(c) Other†.....(036-039)	—	—	—	—	1	3

\*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.  
†Including chancroid, granuloma inguinale and lymphogranuloma venereum.

#### BAT RABIES

##### United States

During the last two months an unusual number of episodes have been reported in which rabid or suspected rabid bats had bitten persons in the central and eastern New York and Pennsylvania areas.

Out of ten biting episodes, laboratory studies on the animals have confirmed rabies in seven of the cases; laboratory diagnosis is pending in two cases, and in one instance the animal was destroyed before studies could be carried out.

In New York state two additional bats were obtained in which rabies was confirmed but which were unassociated with biting episodes.

Pasteur treatment has been administered to those bitten; no human cases of rabies have occurred.

In Pennsylvania, the bats have been identified as the small brown bat (*Myotis lucifugus*). The New York bats are still under study.

#### SMALLPOX

##### Alaska

A smallpox suspected case, an infant about ten months of age, was removed from S.A.S. Flight SK-988 (Tokyo-Anchorage-Copenhagen), at Anchorage on July 8. The patient came from Seoul, Korea. The World Health Organization was notified on July 15 that the suspected case of smallpox at Anchorage had been diagnosed as chickenpox.

Epidemiology Division, Department of  
National Health and Welfare.

Ottawa, August 15, 1961.

## BOOK REVIEWS

**HISTOLOGY**, 4th ed. Arthur W. Ham and Thomas Sydney Leeson. 942 pp. Illust. J. B. Lippincott Company, Montreal, 1961. \$11.00.

Professor Ham is a brave man. When he published the first edition of his book in 1950, he was entering into a field where some of his predecessors were giants. The measure of his success was greatly related to the human and medical appeal of the new text; here was a book for *medical students*, which spoke of histology in terms of their fondest yearnings; here was a book which took them on ward rounds, while it was teaching histology and teaching it well. The present edition, which issues in great part out of the Ontario Cancer Institute, has lost none of its original appeal. For instance, the story of the recent marriage of histology and immunology is beautifully told. T. S. Leeson, the new co-author, is a happy choice, bringing authority to the fields of cytology and ultrastructure. The new chapter on the placenta is a welcome addition.

On the negative side, it seems that the revision has stopped short of the last chapter. The System of Sensory Receptors, particularly the inner ear section, has few references in the '50's and '60's and could be revitalized. Personally, this reviewer would like to see more realistic hematology pictures, particularly since the publisher accepts the expense of colour plates. The reproduction of some illustrations, electron-micrographs especially, is disappointing.

One is grateful to Drs. Ham and Leeson for the Canadian flavour which one finds in their book (even the embryos are from Toronto). This is an honest recognition of the good work done in histology by some of our compatriots. It is indeed heartwarming to read the names of Axelrad, Barr, Bensley, Clermont, Gross, Hamilton, Leblond, Smith, Ste-Marie and so many others.

**VERTEBRAL AND CAROTID ANGIOGRAMS IN TENTORIAL HERNIATIONS**. Including Roentgen Anatomy of the Tentorial Incisure. Hans F. Plaut. 155 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. \$10.50.

This book is of value primarily to the neurologist, neurosurgeon and neuroradiologist. It describes and

demonstrates the angiographic appearances of herniations of cerebral and cerebellar tissue through the incisura tentorii and foramen magnum respectively. In addition, herniation of one cerebral hemisphere to the contralateral side through the opening in the falx cerebri is illustrated.

Much basic research and cadaver dissection have been carried out to prove the angiographic appearance of the various herniations.

The work has been very well prepared and deals with displacements which are difficult to interpret from angiograms.

The subject matter is easily understood and line drawings greatly enhance the value of the roentgenograms.

For those who are engaged in the interpretation of cerebral angiograms, this book will be found exceedingly useful.

**CHEMOTHERAPY OF TUBERCULOSIS**. A Monograph in American Lectures in Living Chemistry. William F. Russell, Jr., and Gardner Middlebrook. 130 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$7.25.

This is an excellent treatise on the chemotherapy of tuberculosis. It is easy reading, and devoid of frills. All of the antituberculous chemotherapeutic agents excepting '1314' (Ethionamide) have been discussed.

Although the laboratory facilities which are available to the authors are not present in every community, the reader will most certainly realize that the initiation of antituberculous drugs to a patient not previously treated is a serious consideration.

It is well documented that meticulous care in selection and administration of antimicrobial agents in the treatment of tuberculosis is indicated. Although the initiation of treatment at home is not mentioned, a survey of the book would lead one to believe that hospitalization is almost mandatory for at least the first six months of treatment.

The book is well worth reading by all physicians interested in tuberculosis, and especially by those less experienced ones who might be considering the treatment of patients at home.

**AN OUTLINE GUIDE FOR THE CARE OF POST-OPERATIVE CARDIAC PATIENTS.** Merle E. White. 106 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. \$6.00.

A text is now available for those wishing to learn about postoperative cardiac patients and, while the book is written by a cardiac nurse chiefly for the nursing profession, surgeons and physicians will find it most instructive.

The author describes the preparation of a recovery room unit, and also outlines the equipment necessary for treatment of a patient returning from cardiac surgery. This aspect is detailed for those patients undergoing closed cardiac procedures and again for open cardiac operations, the latter being more elaborate.

In places, the detail of patient care is excessive and may seem unnecessarily complex. However, the book is an excellent guide to nurses and is based on sound nursing principles. The author outlines the necessary nursing and laboratory procedures for the cardiac patient such as evaluation of vital signs, details of oxygen therapy, estimation of correct fluid balance, required sedation and pertinent blood chemistry.

Indeed, of great value to all medical personnel is a chapter on the specific treatment of postcardiac emergencies, such as cardiac arrest, acute arrhythmias, laryngeal stridor, dyspnea, convulsions, and cerebral embolism.

Moreover, the indications and pharmacological action of drugs used in cardiac emergencies are well reviewed.

A chapter of importance to the cardiac nurse outlines some of the more common cardiac malformations, including symptomatology and surgical therapy, and while this is the weak point of the book, it has much to recommend it.

The book is recommended to all postoperative recovery room personnel and specifically to those engaged in or contemplating nursing postoperative cardiac patients.

**CLINICAL METHODS OF NEURO-OPHTHALMOLOGIC EXAMINATION.** 2nd ed., completely revised and enlarged. Alfred Kestenbaum. 577 pp. Illust. Grune & Stratton, New York; The Ryerson Press, Toronto, 1961. \$18.50.

The first edition of this book, published some years ago, is widely read. This second edition is larger, comprising 577 pages, and illustrates vividly the author's thorough knowledge and great experience in his subject. Neuro-ophthalmology, though extremely important and wide in its scope, is somewhat neglected. This book should stimulate interest in this field among oculists, neurologists, neurosurgeons and internists. It should be required reading for those training in these specialties.

The book is logically planned, starting with a very complete chapter on neuro-ophthalmic anatomy. Throughout the book the author makes full use of tables and drawings to aid the reader in interpreting the text. He also reviews, where and when pertinent, the anatomy of the ocular muscles, the pupillary muscles and version movements.

The classical methods of perimetry are fully discussed, the techniques described and the pitfalls stressed. A strong plea is made for the use of face outline perimetry (Kestenbaum) to replace the customary confrontation test. Useful hints are given to facilitate the plotting of visual fields in the absence of

central fixation. Other less used methods, such as Fluker pattern after-image and stereoscopic and transposition perimetry, are briefly described; these all have their place.

The chapters on extrinsic and intrinsic eye muscles, convergence and divergence derangements, nystagmus and vision movements are of especial interest. In regard to the difficult problem of nystagmus and complicated mechanisms involved, the methods of examination used and associated lesions are meticulously set down.

A short chapter on functional disturbances should stimulate greater interest among non-psychiatrists in these aberrations.

The glossary is extensive, and the definitions are concise but adequate. The bibliography is international and comprehensive, containing hundreds of names reaching back to the immortal Graefe.

There is much in this book which is of interest and education to the novice as well as to the initiated. The format is attractive, the print clear and the size convenient.

**HAEMOPHILIC DISEASES IN DENMARK. A Classification of the Clotting Defects in 78 Haemophilic Families.** Knud-Erik Sjolín. 349 pp. Blackwell Scientific Publications, Oxford; Charles C Thomas, Springfield, Ill., 1961. \$8.50.

Dr. Sjolín presents a study of the clotting defects of 78 hemophilic families of Denmark. This extensive study of the national picture of hemophilic disease will be of interest not only to the geneticist, but also to the hematologist. The book presents a simplified review of the theories of the coagulation mechanism together with a review of the techniques used. Dr. Sjolín has made extensive use of the thrombin generation test in his investigation, and has devoted a whole chapter to this test and the influence of various factors on the generation of thrombin. Although some investigation has been carried out by means of the thromboplastin generation test, the author has found this to be less sensitive in the detection of minor abnormalities than the thrombin generation test. Certain problems arising from the need to transport samples from different parts of the country necessitated a study of the changes induced by storage and freezing on various defects of the clotting mechanism, which were under study.

Among the 156 hemophilic patients investigated, three patients were classified as having PTA deficiency (Rosenthal syndrome) and 11 patients as having a deficiency of Hageman factor. Combined deficiency of antihemophilic factor and Christmas factor was noted in 19 patients, which seems very high, since this combined form of hemophilic disease had been thought to be extremely rare. The occurrence of a seemingly high proportion of a rare disease may be an indication of the sensitivity of the test used. However, it is possible that certain factors, such as the labile serum factor as described by Connor *et al.* (*J. Clin. Invest.*, 40: 13, 1961), may account for this discrepancy.

The author has conducted an extensive study of the broad picture of hemophilic diseases in Denmark and one could only wish that he had been more critical in his assessment of some of the rarities presented.

(Continued on page 862)

CONNAUGHT

# IMMUNE SERUM GLOBULIN (HUMAN)

The production of Immune Serum Globulin (Human) by the Connaught Medical Research Laboratories has been made possible by the cooperation of the Canadian Red Cross Society, the Federal Government and the Governments of each of the Provinces.

Immune Serum Globulin is distributed by Provincial Departments of Health and also by the Canadian Red Cross Society through its regional blood depots for therapeutic purposes only. In addition, Immune Serum Globulin (Human) prepared from blood collected privately is available directly from the Laboratories on a regular sale basis.

Some of the conditions for which Immune Serum Globulin is indicated are:

- |                                 |   |
|---------------------------------|---|
| <b>Measles (rubeola)</b>        | —For prevention and modification.                   |
| <b>Hypogammaglobulinæmia</b>    | —For maintenance of the patient's resistance to     |
| <b>and</b>                      | infection.  |
| <b>Agammaglobulinæmia</b>       |   |
| <b>Infectious Hepatitis</b>     | —For close contacts or in the control of outbreaks. |
| <b>Poliomyelitis</b>            | —For prevention and modification.                   |
| <b>German Measles (rubella)</b> | —For prevention during early pregnancy.             |



**CONNAUGHT MEDICAL RESEARCH LABORATORIES**  
**UNIVERSITY OF TORONTO**  
**TORONTO 4, CANADA**

*Established in 1914 for Public Service through  
Medical Research and the development of  
Products for Prevention or Treatment of Disease.*

*(Continued from page 860)*

**A SHORT MANUAL OF VENEREAL DISEASES AND TREPONEMATOSIS.** 2nd ed. R. C. L. Batchelor and Marjorie Murrell. 316 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1961. \$4.25.

This is the second edition of this manual, written by two venereologists from Edinburgh, Scotland. Chapters on the standard serological tests for syphilis, the uses and side effects of penicillin and also on endemic syphilis, yaws and other treponematoses have been added to bring it nicely up to date.

There are few works which cover the venereal and associated diseases as this does. It is a short 300 pages and easily read. The photographs and diagrams are small but on the whole very good.

This manual is recommended to general practitioners, students, and nurses whose duties are connected with venereal disease. It will take only a few hours for the reader to become much wiser concerning this group of diseases, some of which are still very definitely with us in this country. Also, a knowledge of the treponematoses occurring in the tropics is becoming increasingly important to all physicians.

**PATIENTS' VIEWS OF MEDICAL PRACTICE.** A study of Subscribers to a Prepaid Medical Plan in The Bronx. Eliot Freidson. 268 pp. Russell Sage Foundation, New York, 1961. \$3.75.

This book purports to be "a rather modest empirical study that explored the attitudes and behaviour of patients who have had experience with more than one way of organizing medical practice". The material contained in it is based largely on information obtained through questionnaires which were sent to patients who were taken care of under three types of medical plans.

The first type was the Health Insurance Plan of Greater New York. This plan combines the insurance principle of prepayment with medical care being given by medical groups who agreed to provide medical services during the course of a year for a flat annual sum rather than for a fee for each service. The second group was the Montefiore Hospital Medical Group in the Upper Bronx area of New York. Unlike the H.I.P., this group is not a partnership. All participating physicians are salaried employees of the hospital and members of the hospital staff. The third type of care was given by the Family Health Maintenance Demonstration; 144 eligible families were induced to enter this special program. These families were taken as a random sample from the Montefiore Medical Group and the Demonstration was performed on a team basis. Patients were not only offered the everyday services of a family doctor and pediatrician, but were encouraged to use the services of a social worker and a public health nurse.

"Solo" practice was not specifically studied as such, but by inference, as the patients were questioned on their attitude towards their neighbourhood "solo" practitioner, such as a pediatrician, internist or obstetrician.

This study has a definite value, but one feels that much of the information has been gleaned from an area which is in itself unusual and where the patient-physician relationships are not those that can be found anywhere else outside the Bronx. The questionnaires themselves are interesting, but the questions seem to be "loaded" and it would be interesting to have these

questions circulated in another area; a comparison with the attitudes in the Bronx might be very illuminating.

This book can be recommended to those who are interested in a sociological study of patient-physician relationships in large city areas, and it is to be hoped that further investigation along these lines might be carried out in smaller areas.

**LOCAL ANESTHESIA AND PAIN CONTROL IN DENTAL PRACTICE.** 2nd ed. Leonard M. Monheim. 319 pp. Illust. The C. V. Mosby Co., St. Louis, Mo., 1961. \$8.75.

This volume has been prepared with the stated purpose of stressing the importance of pain control in all phases of dental procedures. To accomplish this aim the author has outlined the requirements of the pre-operative and postoperative periods, in addition to the main theme of regional analgesia.

The book opens with a discussion of pain perception, factors affecting the pain reaction threshold, and accepted methods of pain control. There follows a concise but detailed review of the neuroanatomy of the face and oral cavity which serves to refresh the reader's knowledge of the pathways of innervation to these areas.

The section on injection techniques is presented in a systematic manner, allowing for convenient reference. Each area is dealt with individually under a series of headings which leave no room for doubt regarding the method advocated. Pertinent anatomical landmarks are described in each case.

The many local anesthetic compounds are compared and their pharmacology is discussed. Complications arising from the use of local anesthetic solutions are described and counter-measures or means of prevention are given.

This volume is profusely illustrated with excellent diagrams and photographs which add greatly to its value. While some of the pictures of wet specimens are lacking in clarity, this is more than compensated for by the quality of the accompanying sketches.

This book will be an excellent study text for the undergraduate student, and while it is written primarily for dentists, it would provide a useful reference for the experienced medical practitioner as well.

**INTERNATIONAL WORK IN HEALTH STATISTICS.** 1948-1958. H. S. Gear, Y. Biraud and S. Swaroop. 56 pp. World Health Organization, Geneva, Switzerland, 1961. \$0.60.

These 56 pages present several articles published in the WHO Chronicle from 1959 to 1960, reviewing the history and development of national and international health and vital statistics, pointing out the pitfalls and indicating specifically the contributions made by the World Health Organization. To the list of factors certainly contributing to the decline in typhoid fever mortality, the authors add "and, perhaps, anti-typhoid inoculations (though the part played by inoculations is difficult to assess)"; they mention neither whooping cough vaccine nor typhus vaccine, but give full credit to preventive immunization for the control of diphtheria.

Those who use the records of vital statistics and the many more who should use them will find much of interest in this brief review.

## Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

**The Health of the Aged.** An investigation into the health and a number of social and psychological factors concerning aged persons in the Netherlands, carried out by 374 general practitioners under the direction of the Organization for Health Research, T.N.O. R. J. van Zonneveld. 439 pp. Illust. Van Gorcum & Company, N.V., Assen, The Netherlands, 1961. \$22.50.

**Microbial Reaction to Environment.** Eleventh Symposium of the Society for General Microbiology held at the Royal Institution, London, April 1961. Edited by G. G. Meynell and H. Goshier. Cambridge University Press, London; The Macmillan Company of Canada Limited, Toronto, 1961. \$7.15.

**System of Ophthalmology.** Vol. II. The Anatomy of the Visual System. Stewart Duke-Elder and Kenneth C. Wybar. 901 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1961. \$39.99.

**Pharmacology and Oral Therapeutics.** 12th ed. Edward C. Dolans. 578 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1961. \$10.00.

**Human Pituitary Gonadotropins.** A Workshop Conference. Edited by A. Albert. 434 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$18.50.

**Carter's Principles of Microbiology.** 4th ed. Alice Lorraine Smith. 603 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1961. \$6.00.

**Speech and Hearing Problems.** A Guide for Teachers and Parents. Charles E. Palmer. 133 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$6.00.

**Bile Pigments in Health and Disease.** American Lecture Series. C. H. Gray. 95 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$5.50.

**The Nature of the Genius.** Andrew Gemant. 197 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$7.25.

**Obstetrical Endocrinology.** American Lecture Series. José Botella-Llusá. 124 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$7.25.

**The Exercise Electrocardiogram in Office Practice.** E. Grey Dimond. 169 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$11.00.

**The Parathyroids.** Proceedings of a Symposium on Advances in Parathyroid Research held at The Rice Institute, now Rice University, Houston, Texas. Edited by Roy O. Greep and Roy V. Talmage. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$13.50.

**The Chemistry of Cancer Toxin—Toxohormone.** American Lecture Series. Waro Nakahara and Fumiko Fukuoka. 70 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$4.75.

**The Mystery of Life.** Arnold M. Ludwig. 139 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$6.25.

**Parental Attitudes and Child Behaviour.** Edited by John C. Whitwell. 253 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$9.25.

**A History of Thoracic Surgery.** Richard H. Meade. 901 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$30.25.

**Klinische Chirurgie für die Praxis.** In vier Banden. Band I, Lieferung 5. Edited by O. Diebold, H. Junghanns and L. Lakschwerdt. pp. 937-1087. Illust. Georg Thieme Verlag, Stuttgart, West Germany; Intercontinental Medical Book Corporation, New York, 1961. \$9.75.

**Principles of Medical Statistics.** 7th ed. A. Bradford Hill. 367 pp. Illust. The Lancet Limited, London, 1961. 12s. 6d. net.

**Thoracic Diseases.** Emphasizing Cardiopulmonary Relationships. Eli H. Rubin, Morris Rubin, George C. Leiner and Doris J. W. Escher. 968 pp. Illust. W. B. Saunders Company, Philadelphia; McAlinsh and Company Limited, Toronto, 1961. \$25.00.

**Physiology of the Digestive Tract.** Horace W. Davenport. 221 pp. Illust. Year Book Medical Publishers, Inc., Chicago, Ill., 1961. \$8.50.

**The Cervix Uteri and its Diseases.** C. Frederic Fluhmann. 38 pp. Illust. W. B. Saunders Company, Philadelphia; McAlinsh and Company Limited, Toronto, 1961. \$14.00.

**Recent Contributions to Antibacterial Therapy.** Annals of the New York Academy of Sciences. Vol. 82, Art. 1. pp. 1-190. Conference Chairman: Paul S. Rhoads. The New York Academy of Sciences, New York, 1959. \$2.50.

**Basic Neuroanatomy.** Carlton George Smith. 257 pp. Illust. University of Toronto Press, Toronto, 1961. \$9.00.

(Continued on page 40)

## CLASSIFIED ADVERTISEMENTS

**COMPACT, UNOPPOSED PRACTICE FOR SALE** in town of 500 people in northwestern Manitoba. Ten-bed hospital in town, modern house available. Easy terms. Owner leaving for personal reasons. For details reply to Box 37, CMA Journal, 150 St. George St., Toronto 5, Ont.

**LARGE GENERAL PRACTICE** in central Alberta for sale. 1960 gross income \$30,000. Hospital 15 miles on paved highway. One other doctor in town. Willing to sell for much less than actual real estate value of property. \$5000 downpayment can complete this transaction. Very reasonable terms will be given. Owner wants to specialize. Reply to Box 39, CMA Journal, 150 St. George St., Toronto 5, Ont.

### Residencies and Internships

**PSYCHIATRIC RESIDENCIES.**—Hospital with large medical staff offers fully accredited three year training program beginning July 1, 1962 for men and women graduates of Canadian or American schools desiring certification in psychiatry. Includes postgraduate course, guest lectures, training in modern therapeutic procedures and supervised work in mental hygiene clinics. Liberal salary includes family maintenance. Reply to Box 603, CMA Journal, 150 St. George Street, Toronto 5, Ontario.

**GENERAL HOSPITAL, St. John's, Newfoundland, Canada.** Applications are invited to fill vacancies on the intern staff of the General Hospital, St. John's, Newfoundland. This 456-bed general hospital is approved for intern training by The Canadian Medical Association. Salary is at the rate of \$300 per month, less a deduction of \$47 per month for room and board. An additional allowance of \$50 per month is payable to married applicants with one or more dependents residing in St. John's. Transportation is provided from Canadian centres on the basis of one year's service. Further information can be obtained from The Superintendent, The General Hospital, St. John's, Newfoundland.

**GENERAL HOSPITAL, St. John's, Newfoundland, Canada.** Applications are invited from interested physicians to fill residency posts for postgraduate training commencing January 1, 1962. These are approved by the Royal College of Physicians and Surgeons of Canada. This is a 456-bed acute general hospital, with positions available in medicine, surgery, pediatrics, radiology, pathology, and anesthesia, salary is \$4000 per year. An allowance of \$50 per month is payable to residents with dependents residing in St. John's. Transportation is provided from Canadian and U.K. centres. For further information please contact: The Superintendent, The General Hospital, St. John's, Newfoundland, Canada.

**A 350-BED GENERAL HOSPITAL** offers rotating internship with full teaching program in all services. Remuneration \$250 per month and full maintenance. Apply to Director, Medical Education and Research, The Doctors Hospital, 45 Brunswick Ave., Toronto, Ont.

**PATHOLOGY RESIDENCY.**—4-year approved program in pathologic anatomy and clinical pathology supervised by four pathologists, two biochemists and bacteriologist. 710-bed hospital, over 6000 surgicals and 400 autopsies. Opportunities for research in ultra-micro chemistry and new diagnostic methods; animal research facilities under construction. Apply: Edwin M. Knights, Jr., M.D., Pathology Department, Hurley Hospital, Flint 2, Michigan, U.S.A.

**STATE OF CONNECTICUT, FAIRFIELD STATE HOSPITAL, NEWTOWN, CONN., U.S.A.**—Residents in psychiatry. Applications are invited from men and women graduates of Canadian medical schools for residency training in psychiatry. Large modern hospital with three year training accreditation for American board certification. Active and varied teaching program in affiliation with Yale University. Close to metropolitan areas. Maintenance at nominal cost immediately available for single applicants, waiting list for family accommodations. Beginning stipend \$455 per month. Write giving particulars to Jane E. Oltman, M.D., Director of Training.

**PATHOLOGY RESIDENCIES.**—974-bed private general hospital with progressive teaching and research programs. Fully approved for four years in PA and CP. Four certified pathologists. Surgical—14,740; autopsies—428; total examinations—1,127,965. Indiana University teaching conferences and appointments available. Stipend first year \$4320 (plus dependent child allowances) with annual increases and opportunity for extra income. Housing on premises available. Indiana licensure or permit is necessary. Apply to Dr. Lester H. Hoyt, Director of Clinical Laboratories, Methodist Hospital, Indianapolis 7, Indiana.

**THE OTTAWA CIVIC HOSPITAL, Ottawa, Ontario,** invites applications for resident, assistant resident and junior rotating interns for the 1962-63 term. This is a teaching hospital of approximately 1200 beds plus 125 bassinets, fully accredited by the Canadian Council on Hospital Accreditation and affiliated with the University of Ottawa Medical Faculty. All enquiries should be addressed to Secretary, Intern Committee, Ottawa Civic Hospital, Ottawa, Ontario, Canada.



## BASIC NUMBERS FOR INDIVIDUALIZED PAIN CONTROL

Codeine, combined with acetylsalicylic acid, phenacetin and caffeine, continues to be preferred for the relief of pain. By varying the amount of codeine in this combination, adjustment to individual needs and circumstances is conveniently provided.

**"222"** TABLETS (white)  
Codeine phosphate .....  $\frac{1}{8}$  gr.

**"282"** TABLETS (yellow)  
Codeine phosphate .....  $\frac{1}{4}$  gr.

**"292"** TABLETS (pink)  
Codeine phosphate .....  $\frac{1}{2}$  gr.

*and when codeine is not required*

**"217"** TABLETS—the synergistic formula basic to Frosst analgesic products.

Desage: One or two tablets as required.

☎ Telephone narcotic prescription permitted.

Acetylsalicylic acid ..  $3\frac{1}{2}$  gr.  
Phenacetin .....  $2\frac{1}{2}$  gr.  
Caffeine citrate .....  $\frac{1}{2}$  gr.



**Charles E. Frosst & Co.**  
MONTREAL CANADA

## MEDICAL NEWS in brief

(Continued from page 852)

### PROFESSIONAL PANEL TO ANALYSE CHILDREN'S DRAWINGS

The making of symbols is one of man's primary activities — as natural as eating, moving, or looking about. And when a child unexpectedly emerges from a hap-hazard scribbler to become an artist, it is one of the most exciting moments in his young life. Suddenly he can make marks that have meaning, and he can do it all by himself and whenever he feels like it.

These marks also have meaning to the psychiatrist and psychologist versed in the use of art analysis, for spontaneous drawings by children are being used increasingly as a valuable aid in psychological diagnosis. The way in which a child creates a drawing can tell much about his mental and physical development, and standard analysis techniques, such as the Goodenough test, make it possible to gain insight into personality traits, behaviour patterns, and other mental and physical characteristics.

Increasing interest in this facet of modern medicine by the medical profession has prompted Frank W. Horner Limited to develop a program based on the clinical analysis of children's art. A professional panel composed of a psychiatrist, a clinical psychologist, and an eminent authority on children's art, will analyse drawings that have been collected from practically every geographic location in Canada, from ethnic and socio-economic background, but all from children in the 2-8 year age group. The panel's interpretations of these drawings will be featured in a series to be published by the sponsoring corporation.

The panel will not only consider the psychological aspect of analysis, but will also attempt to evaluate the latent art talent of the child artists, for the beginnings of art for the very young are first of all the learning of muscular control and dexterity in acquiring a new physical skill. The joyful discovery and wonder in what this skill makes possible comes to them only later as they interpret a situation, whether experienced or imagined. This medium of self-expression provides the child with an early sense of individuality . . .

a continuing and gradual development which is a part of growing up.

While these analyses can only be registered in broad terms, the whole program should contribute much toward generating interest in this particular aspect of clinical diagnosis.

#### A NEW VISTA IN PULMONARY CYTOLOGY: AEROSOL INDUCTION OF SPUTUM

There are four principal methods of obtaining bronchial secretions: (1) spontaneous or "natural" cough, (2) bronchial aspiration via the bronchoscope, (3) stimulation of the cough reflex by irritative inhalants and (4) instrumentless flushing of the lower respiratory tract by aerosolized solutions.

Umiker (*Dis. Chest*, 39: 512, 1961) has reported on the application of the latter method to the routine hospital practice of exfoliative cytology. A hygroscopic saline-aerosol technique was used to flush out the bronchial tree. The inhalation was maintained for 10 to 20 minutes and the average amount of nebulized fluid used was 10 to 15 ml. The sputum was expectorated directly into an ether-alcohol mixture. A mean quantity of 10 ml. of sputum was obtained, and in no instance was less than 5 ml. collected. The smears were stained by the standard Papanicolaou method.

Suitable specimens were obtained by artificial induction of sputum from 29 of 31 patients who had previously been unable to raise sputum containing bronchial secretions. These specimens compared favourably with satisfactory spontaneous sputa. Furthermore, they contained more bronchial columnar cells, more pulmonary histiocytes, and fewer cells or debris from the oral cavity and upper respiratory tract.

Among 57 patients who had artificial induction of sputum because of negative smears, and the 31 who had unsatisfactory spontaneous cough specimens, were 29 who eventually proved to have bronchial carcinoma. Malignant cells were recovered from 20 (69%) of these 29 patients by artificial induction of sputum, despite repeated failures with the "natural cough" specimens. In several instances the spontaneous sputum specimens which had been nega-

(Continued on page 42)



## NEW NUMBERS FOR RELIEF OF PAIN PLUS TENSION

These Frosst products permit your prescription of reliable, synergistic "217" analgesia formulations *plus* tension-relieving meprobamate—at usual "217" dosage—without exceeding a *safe total* dosage of meprobamate. In "282 MEP" the benefits of *codeine* are added for more severe pain in the presence of anxiety and/or muscle spasm.

### "217 MEP" TABLETS

Acetylsalicylic acid .....	200 mg.	} PLUS Meprobamate .....	200 mg.
Phenacetin .....	150 mg.		
Caffeine citrate .....	30 mg.		

### "282 MEP" TABLETS

Acetylsalicylic acid .....	200 mg.	} PLUS Codeine phosphate .....	15 mg.
Phenacetin .....	150 mg.		
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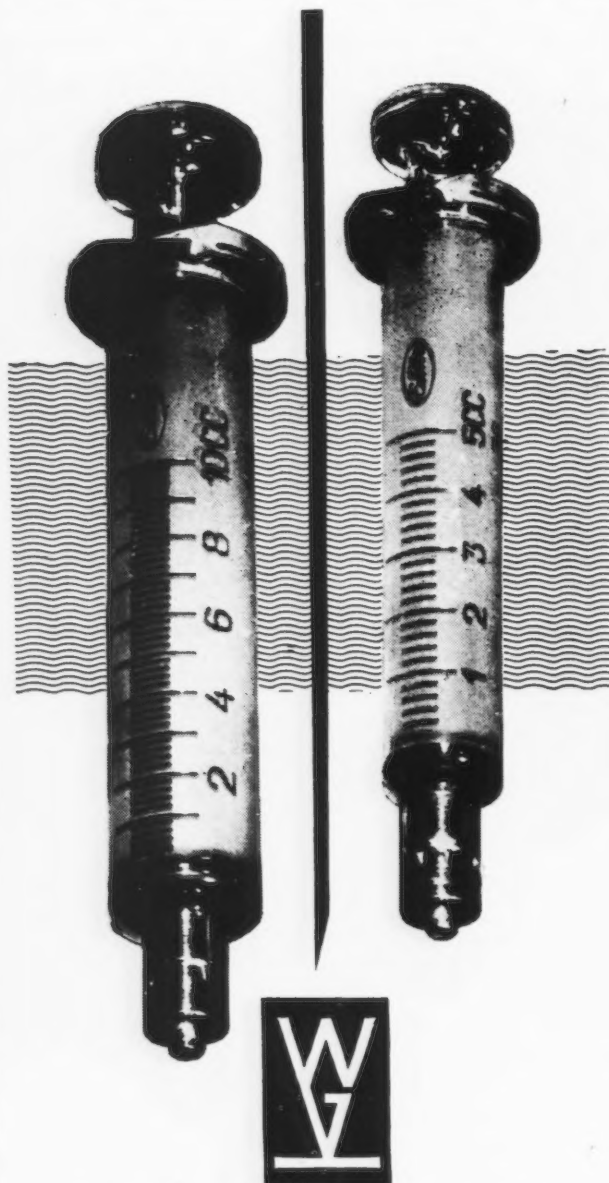
**Dosage:** "217 MEP" and "282 MEP"—One or two tablets every four to six hours as required.

Bottles of 12 and 100 tablets.

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### **Books Received**

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

**Advances in Oto-Rhino-Laryngology.** Rapports II, 7ème Congrès ORL, Paris, Juillet 1961. Edited by J. Leroux-Robert. 323 pp. Illust. S. Karger, Basel, Switzerland; Albert J. Phiebig, White Plains, N.Y., 1961. \$10.00.

**Problems of Estimating Changes in Frequency of Mental Disorders.** Report No. 50. Formulated by the Committee on Preventive Psychiatry. pp. 469-521. Group for the Advancement of Psychiatry, New York, 1961. \$0.75.

**Program Development in the Mental Health Field.** World Health Organization Technical Report Series No. 223. Tenth Report of the Expert Committee on Mental Health. 55 pp. World Health Organization, Geneva; Columbia University Press, New York, 1961. \$0.60. Also published in French and Spanish.

**The Role of Immunization in Communicable Disease Control.** World Health Organization Public Health Papers No. 8. V. A. Zhdanov, R. Cruickshank, E. Edsall and J. de Moerloose. 118 pp. World Health Organization, Geneva; Columbia University Press, New York, 1961. \$1.25. Also published in French.

**The Medicine Show.** Some plain truths about popular remedies for common ailments. The Editors of *Consumer Reports*. 250 pp. Simon and Schuster, Inc., New York; The Mussion Book Company Ltd., Toronto, 1961. \$4.95.

**Teaching of Psychiatry and Mental Health.** World Health Organization Public Health Papers No. 9. Various authors. 186 pp. World Health Organization, Geneva; Columbia University Press, New York, 1961. \$2.00. Also published in French.

**Handbook on Clinical Electromyography.** Robert B. Pearson. 72 pp. Illust. The Meditron Company, El Monte, Cal., 1961. \$2.50.

**The Practical Management of Head Injuries.** John M. Potter. 84 pp. Year Book Medical Publishers, Inc., Chicago, Ill., 1961. \$2.50.

**The Complete Book of Birth Control.** Alan F. Guttmacher, Winfield Best and Frederick S. Jaffe. 152 pp. Illust. Ballantine Books, Inc., New York, 1961. \$0.50.

**Nomina Anatomica.** 2nd ed. International Anatomical Nomenclature Committee. 99 pp. Excerpta Medica Foundation, Amsterdam and New York, 1961. \$3.75.

## **THE BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE, 2nd Edition**

Under the General Editorship of The Rt. Hon. Lord Horder, G.C.V.O., M.D., F.R.C.P. Extra Physician to H.M. The Queen, Consulting Physician to St. Bartholomew's Hospital.

The aim of the ENCYCLOPAEDIA is to meet the very real need of the practitioner for a completely up-to-date guide to which he may turn for the latest information and practical advice on every condition and ailment which could arise in the course of his practice, set out in straightforward style, and carrying the authority of the leading men in medicine today. Thoroughness and accuracy are combined with special attention to practical requirements. Planned on so vast a scale that it covers every aspect of modern medicine, the ENCYCLOPAEDIA is a long-term investment, keeping abreast of the times, and its users may be secure in the knowledge that they will have not only expert advice but up-to-date advice for many years to come.

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**Analgesic potency as great as morphine  
without drowsiness or hypnosis\***



Alvodine, a new and powerful narcotic analgesic, relieves pain as effectively as morphine, yet is much safer because it is free from the high incidence and severity of morphine's side effects. Alvodine is effective *orally* as well as parenterally. Alvodine causes almost no sedation, drowsiness or euphoria. Respiratory and circulatory depression are rare with customary doses; nausea and vomiting are uncommon. Constipation has not been reported.

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**How Supplied:** Alvodine tablets, 50 mg., scored. Alvodine ampuls, 1 cc., containing 20 mg. per cc. *Narcotic Blank Required.*



Write for Alvodine brochure containing detailed information on clinical experience, addiction liability, side effects and precautions.

\*In more than 90% of patients.

## MEDICAL NEWS in brief

(Continued from page 39)

tive before artificial induction of sputum became positive after this procedure.

Among 17 patients who had equivocal cytologic reports on the basis of examination of sputum collected by the conventional method, artificial induction of sputum provided sufficient supplemental information in seven instances to permit a more definite categorization, as either positive or negative.

These results indicate that the secretions obtained in aerosol-induced sputum are superior not only to spontaneously raised sputum but also to bronchial aspirates.

The method is recommended for routine hospital, outpatient and office practice.

## TRENDS IN ACCIDENTAL DEATHS

The rate of accidental deaths has decreased in recent years in every geographic division of the U.S.A.,

according to statisticians of the Metropolitan Life Insurance Company.

The greatest improvement was shown by the residents of the east north central area, where the accident death rate fell from 61.8 per 100,000 population in 1949-50 to 50.1 in 1957-58. This decrease was about one-fifth, or nearly twice the relative reduction for the country as a whole. Second best was the Pacific division, where the rate decreased 14%.

In contrast, seven states — all of them in the south and southwest — actually recorded increases in accident death rates during the eight-year period.

The rate of fatal falls diminished by about one-fifth in the nation as a whole, but continued highest in the northeastern section of the country where the proportion of older people in the population is high.

The frequency of drownings dropped by 12% for the United States as a whole, although the trend varied markedly among geographical divisions. The greatest relative improvement occurred in the northeastern and the mid-western sections, whereas the rate increased in a belt of states extending southward from Tennessee and North Carolina and westward through Oklahoma.

Death rates from fire, and burns by other means, decreased by as much as one-third in the Mountain area and one-fourth in the west north central and Pacific divisions. The trend, however, has been upward in many southern states where the number of such deaths has long tended to be relatively high.

Mortality from motor vehicle accidents is in sharp contrast to mortality from the other major causes. The rate increased in a majority of states; the rise was most marked in Louisiana where it jumped by one-third during the eight-year period. The rate changed little in the Mountain states, where it is higher than in any other geographical division. More than 40 persons per 100,000 population were killed in New Mexico and Nevada in 1957-58.

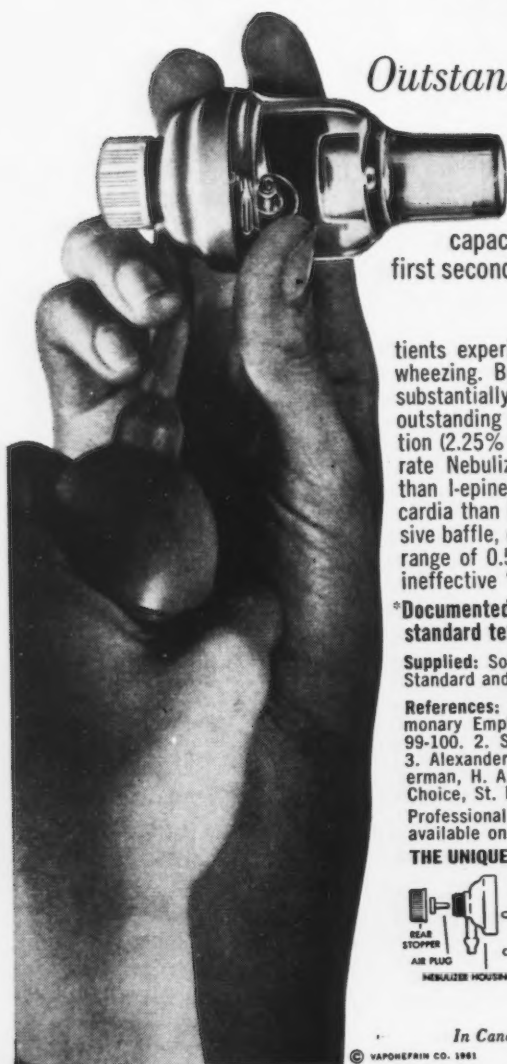
Only in the east north central states did the rate of motor vehicle fatalities drop materially. The highest reduction—one-fifth—was recorded in Michigan.

for asthma, emphysema, chronic bronchitis

INSPIRED RELIEF IN SECONDS<sup>1</sup>

# VAPONEFRIN<sup>®</sup>

A Textbook Therapy for Asthma\*



*Outstanding for effectiveness,  
safety, stability*

"...the greatest improvement [in vital capacity-time relationship] occurs during the first second."<sup>1</sup>

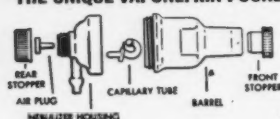
After just 3 to 6 puffs of Vaponefrin, patients experience a marked abatement in dyspnea and wheezing. Bronchospasm is relieved and vital capacity substantially increased within a few minutes.<sup>1-3</sup> These outstanding clinical benefits result from a superior solution (2.25% racemic epinephrine), and from a more accurate Nebulizer. The solution is safer and more stable than l-epinephrine, and is less likely to produce tachycardia than isoproterenol.<sup>4</sup> The Nebulizer, with its exclusive baffle, consistently produces particles in the critical range of 0.5 to 3 microns<sup>1</sup>—a penetrating mist, not an ineffective "rain".

\*Documented by 163 published clinical evaluations and standard textbook references.

Supplied: Solution, bottles of 7.5, 15 and 30 cc.; Nebulizers, Standard and Pocket size. Also Aerosol Unit.

References: 1. Segal, M. S., and Dulfano, M. J.: Chronic Pulmonary Emphysema, New York, Grune & Stratton, 1953, pp. 99-100. 2. Segal, M. S., and Dulfano, M. J.: GP 7:57, 1953. 3. Alexander, J. K., et al.: Circulation 18:235, 1958. 4. Bickerman, H. A., and Barach, A. L., in Modell, W., Ed.: Drugs of Choice, St. Louis, The C. V. Mosby Company, 1958-59, p. 582. Professional literature and complimentary demonstration set available on request.

## THE UNIQUE VAPONEFRIN POCKET NEBULIZER



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(Continued on page 47)

**MEDICAL NEWS in brief**  
(Continued from page 42)

**IDIOPATHIC HYPERLIPEMIA  
AND ISCHEMIC HEART  
DISEASE**

Idiopathic hyperlipemia is an innate error of lipid metabolism, characterized clinically by a very high incidence of myocardial infarction and chemically by marked elevations of the serum values for triglyceride in the fasting state. In recent times it has become apparent that even in the absence of this familial disorder, patients with ischemic cardiac disease show elevated values for triglyceride, as distinct from the commonly recognized hypercholesterolemia found in such patients.

These similarities stimulated a study by Brown (*Ann. Int. Med.*, 54: 646, 1961) of triglyceride metabolism in four patients with idiopathic hyperlipemia, 15 patients with previous myocardial infarctions, and 15 normal control subjects of corresponding ages. After overnight fasting, each subject drank a half pint of thick cream, containing  $I^{131}$ -labelled fat. Specimens of blood were obtained at intervals during the next 24 hours, and the lipid values in those specimens were measured.

The four patients with idiopathic hyperlipemia showed very marked and abnormally prolonged postprandial lipemia. Similar but less marked abnormalities were observed in patients with ischemic heart disease. The use of radio-

active fat revealed that 24 hours after the ingestion of the cream, the patients with ischemic heart disease retained 0.5% and the normal subjects 0.2% of the ingested dose. The values indicated that all of the morbid subjects in this study were incapable of eliminating ingested triglyceride from the serum with normal speed.

In contradistinction to the observation made by others that lipemia augments coagulability, interferes in the acceptance of oxygen by the tissues, and reduces myocardial blood flow, the present figures give support to the hypothesis that an abnormality of triglyceride metabolism is directly implicated in the pathogenesis of myocardial infarction. The figures also support the recommendation that dietary triglyceride should be restricted as much as possible as a therapeutic and prophylactic measure in cases of ischemic heart disease.

After a considerable reduction in the values for serum triglyceride was brought about by means of a low fat diet in patients with idiopathic hyperlipemia, repetition of the fat tolerance test in two of these individuals revealed that the elimination of ingested triglyceride remained grossly defective. In two subjects the clearance was not substantially improved by the administration of heparin, although it has been demonstrated that this substance produces a high concentration of lipoprotein lipase in subjects who have been investigated.

(Continued on page 50)

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*Decongestant/Antihistamine*

## THE POTENTIATED DECONGESTANT



**provides symptomatic relief of nasal congestion and rhinorrhea of allergic or infectious origin.**

Many patients whose symptoms are inadequately controlled by decongestants or antihistamines alone respond promptly and favorably to 'ACTIFED.'

'ACTIFED' contains:	in each	in each tsp.
	Tablet	Syrup
'Actidil' brand Triprolidine Hydrochloride	2.5 mg.	1.25 mg.
'Sudafed' brand Pseudoephedrine Hydrochloride	60 mg.	30 mg.

**Since 'Actifed' has a wide margin of safety, dosage may be individually adjusted to provide optimal therapeutic effect on stubborn unresponsive cases.**



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HELPS THE  
PATIENT  
"BE HIMSELF"  
AGAIN...CALM.  
YET FULLY  
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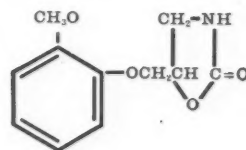
TREPIDONE Mephenoxalone is a new tranquilizer which has shown the capacity to relieve mild to moderate anxiety and tension without detracting significantly from mental alertness. Treated patients have shown little tendency to become sleepy or detached from reality, or to experience euphoria as a result of the drug. They generally respond normally to everyday situations . . . require fewer restrictions on activities, and tend to complain less frequently.

Extensive trials have shown no habit-forming properties or adverse effects on withdrawal, even after long-term administration. For complete information on indications, dosage, precautions and contraindications consult your Lederle representative, or write to our Medical Director, Dr. R. G. Warminton.

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*chemically distinct  
from previous tranquilizers*



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## MEDICAL NEWS in brief

(Continued from page 47)

**PREGNANCY AND  
TUBERCULOSIS**

Before the antimicrobial era in the treatment of tuberculosis the literature expressed conflicting views on the effect of pregnancy on this disease. Since the introduction of chemotherapy very few controlled studies of this problem have been reported, and only a few of those reported have included a prolonged follow-up of the patients.

Mehta (*Dis. Chest*, 93: 505, 1961) undertook to compare a series of patients in whom pregnancy and active tuberculosis co-existed, and who were followed up for a prolonged period of time, with a similar number of non-pregnant women with active tuberculosis, in order to determine whether or not pregnancy has any untoward effect on women whose tuberculosis has been treated, by present standards, with adequate chemotherapy.

The results in 53 patients in whom pregnancy and active tuberculosis co-existed are compared with those in 53 non-pregnant patients with active tuberculosis who were of the same age group and disease status. There was no significant difference in the groups in sputum conversion, roentgenographic improvement and stabilization, cavity closure, or rate of relapse, either early or late. This is in accordance with other recent studies which show that pregnancy has no deleterious effect on tuberculosis when the infection is treated by adequate and prolonged chemotherapy and surgical procedures when indicated. It also stresses the importance of prenatal radiographs of the chest.

**PURULENT MENINGITIS OF  
NEWBORN INFANTS:  
11-YEAR EXPERIENCE IN  
THE ANTIBIOTIC ERA**

Groover, Sutherland and Landing have reviewed 39 cases of neonatal meningitis (16 premature and 23 full-term infants) at the Children's Hospital of Cincinnati and the Cincinnati General Hospital for the period January 1, 1948, to December 31, 1959 (*New England J. Med.*, 264: 1115,

1961). The infants had a positive culture from the cerebrospinal fluid, increased cells in the spinal fluid, an elevated protein and a lowered sugar value (with or without a positive culture) or post-mortem evidence of purulent meningitis, were less than 28 days old at the time of onset of disease, and had no central nervous system anomalies.

The calculated incidence of the cases from the Cincinnati General Hospital was 2.2 per 1000 births of premature infants and 0.13 per

1000 births of full-term infants. The sex incidence was not significantly different.

Enterobacilli were found to be the predominant etiological agents, but Gram-positive cocci were the etiological agents in a significant number of cases.

The onset of meningitis was earlier in premature infants. It was significantly earlier in infants with abnormal perinatal histories, and occurred before six days in all infants whose mothers were febrile or in whom the membranes had

after 4½ years of  
clinical experience  
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“Phenformin is most useful in maturity-onset, stable adult diabetics. The high percentage of cases in which it is clinically satisfactory, the ease and simplicity of its administration in ketosis-resistant cases of diabetes, and the maintenance of long-term response without secondary failure have been impressive.”



ruptured prematurely. There was no significant difference in the age at onset of enteric versus coccal infections. In all cases the clinical findings were vague and non-specific, but they were especially so in the smaller infants. However, the absence of the Moro response indicated a poor prognosis, and the presence of fever indicated a good prognosis.

In this series the mortality rate was 66.6%; it was higher in premature infants (81%) than in full-term infants (57%). The earlier

the symptoms appeared, the worse was the prognosis.

The necessity for early diagnosis and treatment is clear from the report: the earlier specific therapy was begun, the better the prognosis. Although initial treatment should be directed towards both Gram-positive and Gram-negative organisms, subsequent therapy should be based on the results of careful bacteriological studies. Blind therapy is unwise, for it may mask infection and delay definitive diagnosis and treatment.

## IDIOPATHIC NONTROPICAL SPRUE (MALABSORPTION SYNDROME)

Nontropical sprue, a chronic remittent disease characterized by impaired absorptive and motor functions of the small intestine resulting in multiple, often serious, nutritional deficiencies, lacks gross pathological changes, but does exhibit characteristic abnormalities of the mucosa of the upper part of the small intestine which may be specific. Nontropical sprue must be distinguished from sprue syndromes secondary to other diseases that interfere with the function of the small bowel. Evidence indicates that nontropical sprue in adults is the same as celiac disease in infants and children. Although the cause of sprue is not known, there is considerable evidence to suggest that the disease may arise from some hereditary abnormality of the small bowel. The symptoms of sprue may develop as the result of this basic lesion alone, or they may be precipitated by one or more additional inciting factors (dietary deficiencies, intestinal infections, or sensitivity to gluten). Thus, a patient's response to treatment would depend upon the severity of the underlying hereditary defect and the degree to which the correctable inciting causes are responsible for the total clinical picture.

Many patients with nontropical sprue respond satisfactorily to treatment with a diet restricted in fat, rich in protein and supplemented with extra vitamins and minerals. The gluten-free diet, although not always successful, may produce satisfactory results, and may be particularly useful for some patients who do not respond to conventional therapy. Adrenal cortical steroids, usually administered on a temporary basis, have been helpful in establishing remissions in certain treatment-resistant patients.

Although most patients with sprue respond satisfactorily to some sort of medical therapy, the disease has not been completely or permanently cured by any treatment employed. For this reason it is advisable that supplementary vitamins and minerals should be prescribed in all cases.—E. E. Wollaefer and P. A. Green: *Am. J. Gastroenterol.*, 35: 569, 1961.

## "most useful" in stable adult diabetes<sup>1</sup>

Reporting on continuous daily administration in 128 diabetics—in many for up to 4½ years—Pomeranze<sup>1</sup> found DBI the "most valuable of the oral blood-sugar lowering agents" because it is...

"singularly effective" in the control of maturity-onset stable adult diabetes.

no clinical toxicity in long-term use of DBI, as demonstrated by previous studies, is "confirmed by our observations extending over 54 months."

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Rely on DBI for more satisfactory oral regulation of...

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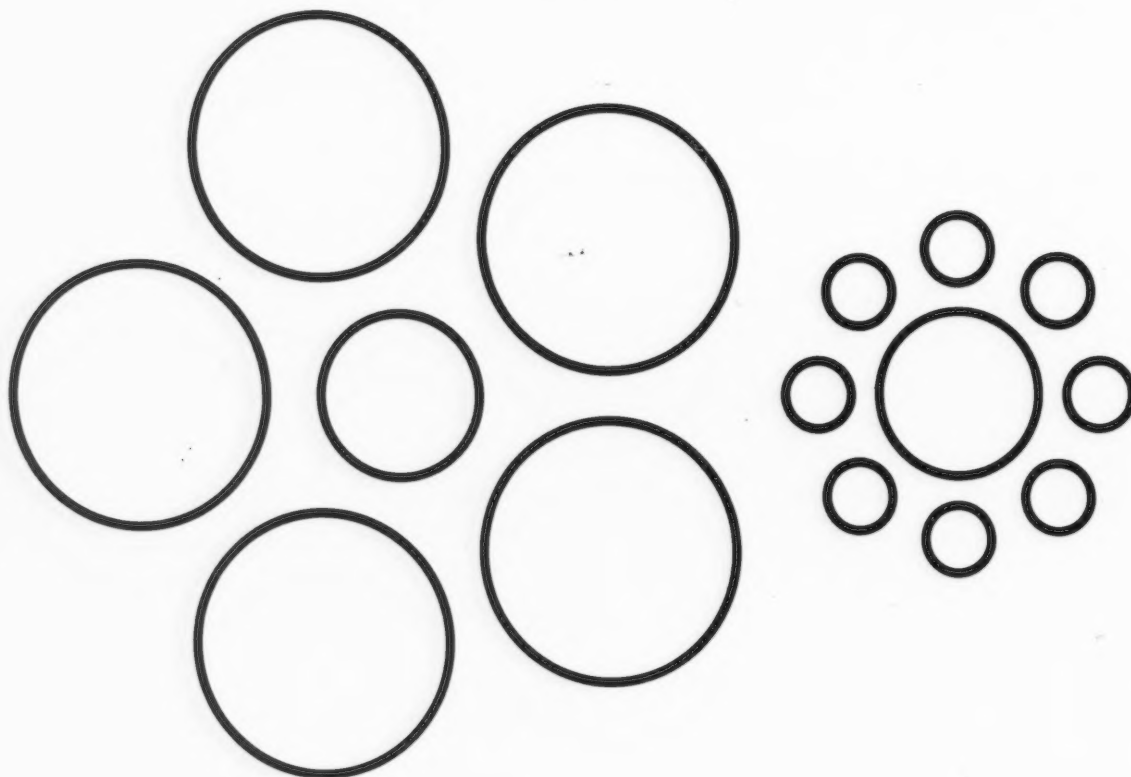
1. Pomeranze, J.: *Clinical Med.* 8:1155, June 1961.

# DBI

(Phenformin HCl)



## which center circle is larger?



Surprising . . . how the circle in the figure at right seems larger than the one at the left—even when you know they're both the same.

Another illusion takes place when we try to compare two oral penicillins. If only the price of the drugs were to be considered, the choice would be clear. But isn't it what a drug *does* that counts?

V-Cillin K® provides greater serum levels of antibacterial activity (ABA) against the streptococcus and the pneumococcus than do other penicillins now available.<sup>1,2</sup> Although staphylococci vary in their susceptibility to penicillin, V-Cillin K provides potent anti-staphylococcus activity. Moreover, it is highly stable in gastric acid and, therefore, more completely absorbed *even in the presence of food*. Your patient gets more dependable therapy for his money . . . and it's therapy—not tablets—he really needs.

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prescribe V-Cillin K in scored tablets of 125 and 250 mg.  
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V-Cillin K® (penicillin V potassium, Lilly)

1. McCarthy, C. G., and Finland, M.: New England J. Med., 263:315, 1960.

2. Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.



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TORONTO, ONTARIO